A DISSERTATION ON

A STUDY ON CLINICOPATHOLOGICAL EVALUATION OF SOLITARY NODULE THYROID

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CERTIFICATE

This in to certify that the dissertation work titled **"A STUDY ON CLINICOPATHOLOGICAL EVALUATION OF SOLITARY NODULE THYROID"** is a bonafide research work of **DR. R.KRISHNA KUMAR** Enrolment No.
submitted in partial fulfillment of the requirements for the award of Degree of **M.S. GENERAL SURGERY** in THE TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY CHENNAI- 600 032

Signature of unit Chief

Signature of H.O.D

Signature of Dean

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INTRODUCTION

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Nodular thyroid disease is a common disorder & the incidence increases with age. The prevalence of nodular goitre is 4-7%, but the autopsy studies & USG have shown that the true incidence is to be around 50% in the adult population. Most thyroid nodules are benign & most of them are adenomas. Although a majority of the nodules are benign & some are shown to be malignant. Thyroid cancers are comparatively rare disorders.

Preoperative identification & evaluation of these nodules is very important. But this distinction often proved difficult with the reliance on the clinical assessment & investigations of low sensitivity & specificity. According to the clinical diagnosis and most importantly tissue diagnosis, the treatment approach can be modified.

The FNAC is said to be the gold standard for the diagnosis of SNG, but the FNAC has got its own pitfalls because of false negatives & false positives reports & the same time the results have inter-observer variation & need an experienced histopathologist. Even FNAC has got less specificity in identifying the micro-papillary projection & can't differentiate between follicular adenoma & carcinoma.

The uses of USG & radioisotope studies are often additive but not much of value in confirming the diagnosis particularly in malignancy. So

surgery of any type plays an important role in the treatment as well as the diagnostic aspect but the present trend is to manage benign lesion on FNAC with conservative line of management reserving surgery for the malignant lesions & suspected malignancies.

AIM OF THE STUDY

AIM

- ✓ To review data regarding **incidence** of the solitary nodular goitre
- ✓ To analyse & discuss the various **clinical presentation**
- ✓ To find out the **percentage of malignancy** in solitary nodular goitre
- ✓ To confirm the **role of surgery** as the diagnostic & therapeutic modality & to discuss the revised indication for surgeries
- ✓ To stress the **importance of histopathological examination** as the final & confirmatory evidence of diagnosis
- ✓ To analyse **the pattern of disease affecting SNG** based on HPE
- ✓ To **compare** the data from this study with the other established studies

REVIEW OF LITERATURE

SURGICAL ANATOMY

Historical Background

Goiters (from the Latin *guttur*, throat), defined as an enlargement of the thyroid, have been recognized since 2700 B.C. In 1619, Hieronymus Fabricius ab Aquapendente recognized that goiters arose from the thyroid gland. The term thyroid gland (Greek *thyreoeides*, shield-shaped) is, however, attributed to Thomas Wharton in his *Adenographia* (1656). Burnt seaweed was considered to be the most effective treatment for goiters.

The most notable thyroid surgeons were Emil Theodor Kocher (1841–1917) Theodor Billroth (1829–1894), who performed thousands of operations with increasingly successful results. After total thyroidectomy, patients (children) became myxedematous with cretinous features. Myxedema was first effectively treated in 1891 by George Murray, who used a subcutaneous injection of an extract of sheep's thyroid; later, Edward Fox demonstrated that oral therapy was equally effective. In 1909, Kocher was awarded the Nobel Prize for medicine in recognition "for his works on the physiology, pathology, and surgery of the thyroid gland."

General Topography: The thyroid gland consists typically of two lobes, a connecting isthmus, and an ascending pyramidal lobe. One lobe, usually the right, may be smaller than the other (7 percent) or may even be completely

absent (1.7 percent). The isthmus is absent in about 10 percent of thyroid glands, and the pyramidal lobe is absent in about 50 percent. A minute epithelial tube or fibrous cord, the thyroglossal duct, almost always extends between the thyroid gland and the foramen cecum of the tongue.

The thyroid gland normally extends from the level of the 5th cervical vertebra to the body of the 1st thoracic vertebra. It may lie higher (lingual thyroid), but rarely lower. The normal thyroid gland weighs about 30 g in the adult —somewhat more in females than in males. Each lobe is approximately 5 cm in length, 3 cm at its greatest width, and 2-3 cm thick. The isthmus connecting the two lobes is about 1.3 cm in breadth. The lobes have a broad lower portion and a relatively conical apex.

Embryogenesis

Normal Development

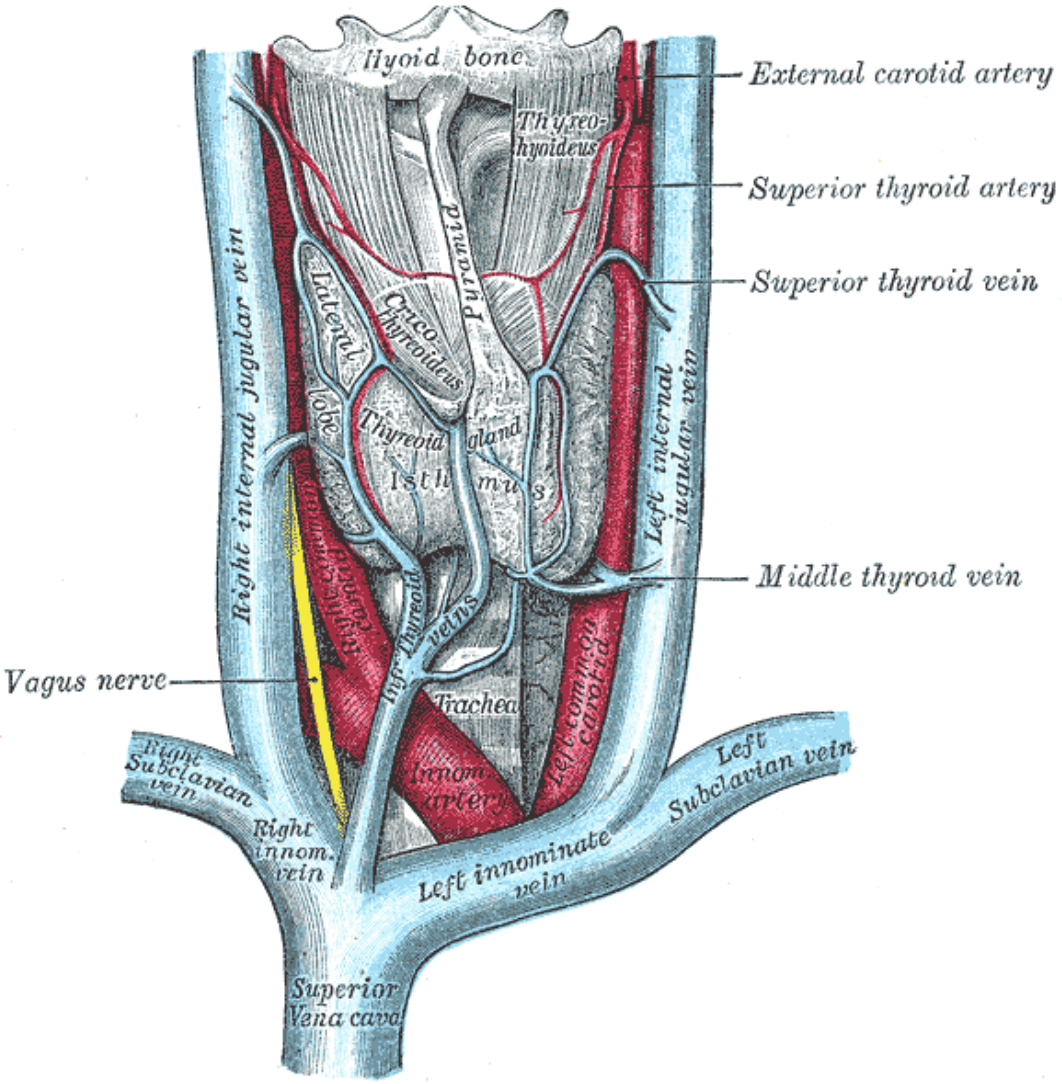
The thyroid gland appears by the end of the third week as an epithelial thickening of the floor of the pharynx at the level of the first pharyngeal pouch. This, the large median thyroid anlage, may be a diverticulum or a solid bud. Cranial growth of the tongue, together with elongation of the embryo, carries the origin of the thyroid gland far cranial to the gland itself. The site of this origin is the foramen cecum of the adult tongue. In some individuals it is not grossly visible.

The thyroid gland remains connected with the foramen cecum by a minute, solid thyroglossal duct that passes through, or anterior to, the hyoid bone. By the fifth week of gestation, this duct usually becomes fragmented; persistence of any portion is not unusual. In about 50 percent of the population, the duct can be traced distally to the pyramidal lobe of the thyroid gland. The developing gland, at first an irregular plate, develops two lateral wings connected by the isthmus. Follicles appear during the second month of gestation and increase through the fourth month. Colloid formation and uptake of radioactive iodine begin at about the eleventh week.

Epithelial structures, the paired lateral anlages, are formed from the ventral portions of the fourth and fifth branchial pouches. This structure, the well-known ultimobranchial body (caudal pharyngeal pouch complex), becomes lost in the developing thyroid gland, and its cells become dispersed as the C (calcitonin) cells among the thyroid follicles.

Present evidence suggests that the primary origin of the calcitonin-producing cells of the thyroid gland is the neural crest of the embryo. From the neural crest these cells migrate to the ultimobranchial body, and later become part of the thyroid gland.

THYROID ANATOMY



Capsule of the Thyroid Gland

The thyroid gland has a connective tissue capsule which is continuous with the septa, and which makes up the stroma & is the true capsule of the thyroid. External to the true capsule is a layer of fascia derived from the pretracheal fascia. This is the false capsule, also called the perithyroid sheath or surgical capsule. Anteriorly and laterally this fascia is well developed; posteriorly it is thin and loose, permitting enlargement of the thyroid gland posteriorly. There is a thickening of the fascia that fixes the back of each lobe to the cricoid cartilage. Such thickenings are the ligaments of Berry. The false capsule, or fascia, is not removed with the gland during thyroidectomy.

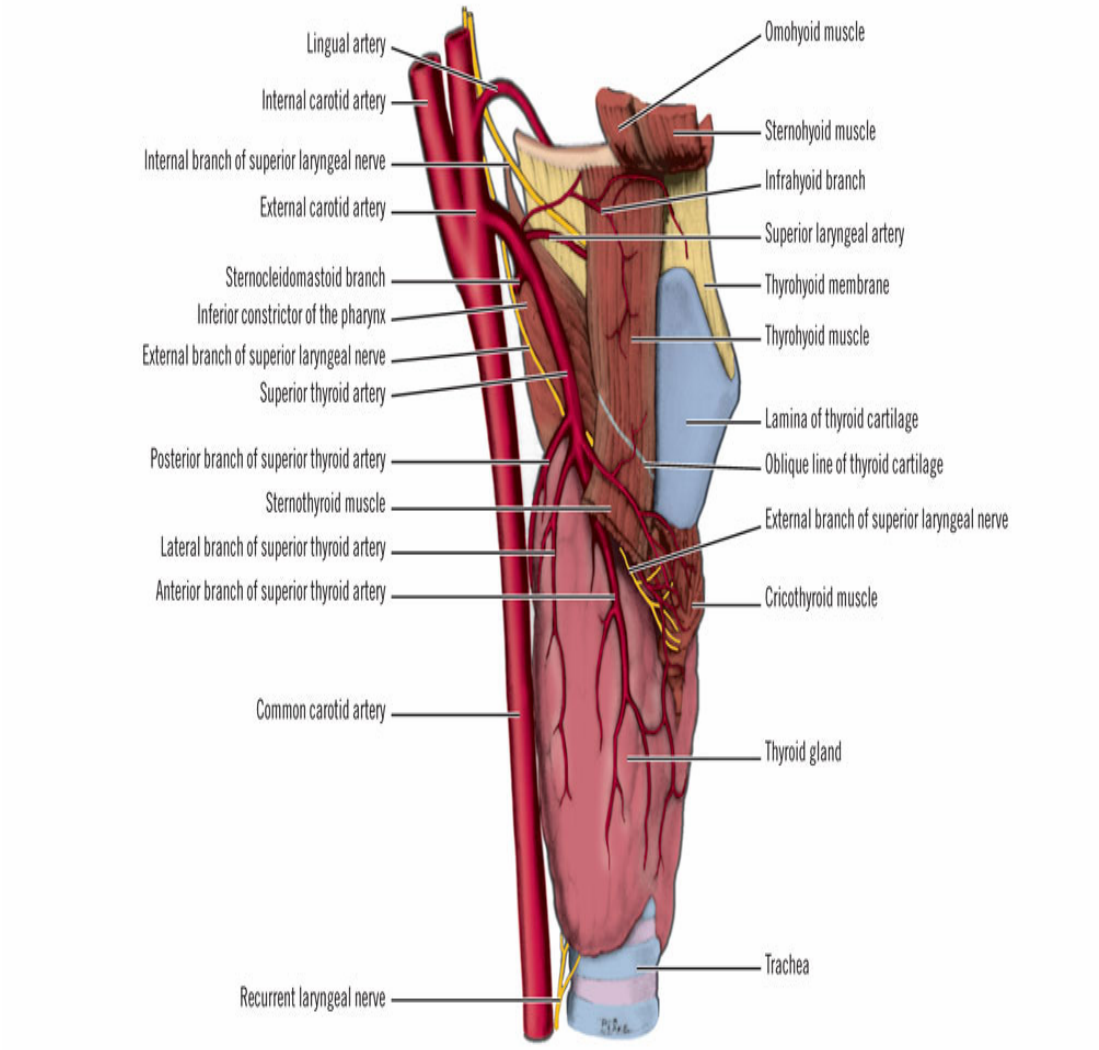
The superior parathyroid glands normally lie between the true capsule of the thyroid and the fascial false capsule. The inferior parathyroids may be between the true and false capsules, within the thyroid parenchyma, or lying on the outer surface of the fascia.

Vascular Supply

The thyroid gland competes with the adrenal glands for having the greatest blood supply per gram of tissue.

Arteries: Two paired arteries, the superior and inferior thyroid arteries, and an inconstant midline vessel, the thyroid ima artery, supply the thyroid.

LATERAL VIEW OF THYROID GLAND



Superior Thyroid Artery: The superior thyroid artery arises from the external carotid artery just above, at, or just below the bifurcation of the common carotid artery. It passes downward and anteriorly to reach the superior pole of the thyroid gland. In part of its course, the artery parallels the external branch of the superior laryngeal nerve which supplies the cricothyroid muscle and the cricopharyngeus muscle, the lowest voluntary part of the pharyngeal musculature. There are six branches of the superior thyroid artery: the infrahyoid, sternocleidomastoid, superior laryngeal, cricothyroid, inferior pharyngeal constrictor, and terminal branches of the artery for the blood supply of the thyroid and parathyroid glands. Usually there are two branches to the thyroid —the anterior and posterior— but occasionally there may be a third, the so-called lateral branch.

At the superior pole, the superior thyroid artery divides into anterior and posterior branches. The anterior branch anastomoses with the contralateral artery. The posterior branch anastomoses with branches of the inferior thyroid artery. From the posterior branch, a small parathyroid artery passes to the superior parathyroid gland.

Inferior Thyroid Artery: The inferior thyroid artery usually arises from the thyrocervical trunk, but in about 15 percent of individuals it arises directly from the subclavian artery. After piercing the prevertebral fascia, the artery

divides into two or more branches as it crosses the ascending recurrent laryngeal nerve.

The recurrent laryngeal nerve may pass anterior or posterior to the artery, or between its branches. The lowest branch sends a twig to the inferior parathyroid gland and supplies the lower pole of the thyroid gland. The upper branch supplies the posterior surface of the gland, usually anastomosing with a descending branch of the superior thyroid artery.

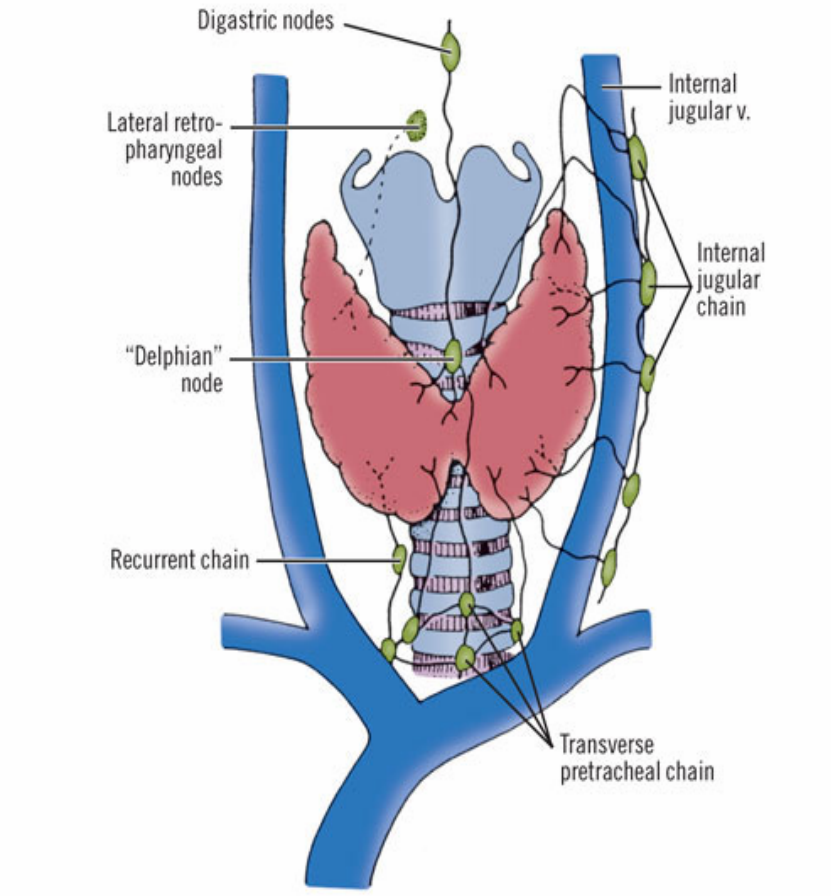
Thyroid Ima Artery: The thyroid ima artery is unpaired and inconstant. It arises from the brachiocephalic artery, the right common carotid artery, or the aortic arch. It occurs in about 10 percent of individuals. Its position anterior to the trachea makes it important in tracheostomy.

Veins

Veins of the thyroid gland form a plexus of vessels lying in the substance and on the surface of the gland. The plexus is drained by three pairs of veins, the superior, middle, and inferior thyroid veins.

Superior Thyroid Vein: The superior thyroid vein accompanies the superior thyroid artery. Emerging from the superior pole of the thyroid, the vein passes superiorly and laterally across the omohyoid muscle and the common carotid artery to enter the internal jugular vein alone or with the common facial vein.

LYMPHATIC DRAINAGE



Middle Thyroid Vein: No artery accompanies it. It crosses the common carotid artery to open into the internal jugular vein. This vein may be absent or, occasionally, double. The extra vein is inferior to the normal one; it has been called the "fourth" thyroid vein. The importance of these middle thyroid veins is in their vulnerability during thyroidectomy.

Inferior Thyroid Vein: The right vein leaves the lower border of the thyroid gland, passes anterior to the brachiocephalic artery, and enters the right brachiocephalic vein. The left vein crosses the trachea to enter the left brachiocephalic vein. Rarely, the right vein crosses the trachea to enter the left brachiocephalic vein, sometimes forming a common trunk with the left vein. This common trunk is called the thyroid ima vein.

Lymphatic System: The thyroid gland is endowed with an extensive network of lymphatics. Intraglandular lymphatic vessels connect both thyroid lobes through the isthmus and also drain to perithyroidal structures and lymph nodes. Regional lymph nodes include pretracheal, paratracheal, perithyroidal, recurrent laryngeal nerve, superior mediastinal, retropharyngeal, oesophageal, and upper, middle, and lower jugular chain nodes. These lymph nodes can be classified into seven levels. The central compartment nodes located in the area between the two carotid sheaths, whereas nodes lateral to the vessels are present in the lateral compartment.

Nerves: The left RLN arises from the vagus nerve where it crosses the aortic arch, loops around the ligamentum arteriosum and ascends medially in the neck within the tracheoesophageal groove. The right RLN arises from the vagus at its crossing with the right subclavian artery. The nerve passes posterior to the artery before ascending in the neck, its course being more oblique than the left RLN. Along their course in the neck, the RLNs may branch, and pass anterior, posterior or interdigitate with branches of the inferior thyroid artery. The right RLN may be nonrecurrent in 0.5 to 1% of individuals and is often associated with a vascular anomaly in this situation. Nonrecurrent left RLNs are rare, but have been reported in patients with situs inversus and a right-sided aortic arch. The RLN may branch in its course in the neck, and identification of a small nerve should alert the surgeon to this possibility. Identification of the nerves or their branches often necessitates mobilization of the most lateral and posterior extent of the thyroid gland, the tubercle of Zuckerkandl, at the level of the cricoid cartilage. The last segments of the nerves often course below the tubercle and are closely approximated to the ligament of Berry. Branches of the nerve may traverse the ligament in 25% of individuals, and are particularly vulnerable to injury at this junction. The recurrent laryngeal nerves terminate by entering the larynx posterior to the cricothyroid muscle.The RLNs innervate all the intrinsic muscles of the larynx, except the cricothyroid muscles, which are innervated by the external laryngeal nerves.

Injury to one RLN leads to paralysis of the ipsilateral vocal cord, which comes to lie in the paramedian or the abducted position. The paramedian position results in a normal, but weak voice, whereas the abducted position leads to a hoarse voice and an ineffective cough. Bilateral RLN injury may lead to airway obstruction, necessitating emergency tracheostomy, or loss of voice. If both cords come to lie in an abducted position, air movement can occur, but the patient has an ineffective cough and is at increased risk of repeated respiratory tract infections from aspiration.

The superior laryngeal nerve:The superior laryngeal nerves also arise from the vagus nerves. After their origin at the base of the skull, these nerves travel along the internal carotid artery and divide into two branches at the level of the hyoid bone. The internal branch of the superior laryngeal nerve is sensory to the supraglottic larynx. Injury to this nerve is rare in thyroid surgery, but its occurrence may result in aspiration. The external branch of the superior laryngeal nerve lies on the inferior pharyngeal constrictor muscle and descends alongside the superior thyroid vessels before innervating the cricothyroid muscle. Cernea and associates proposed a classification system to describe the relationship of this nerve to the superior thyroid vessels. The type 2a variant, in which the nerve crosses below the tip of the thyroid superior pole, occurs in up to 20% of individuals and places the nerve at a greater risk of injury. Therefore, the superior pole

vessels should not be ligated en masse, but should be individually divided, low on the thyroid gland, and dissected lateral to the cricothyroid muscle. This nerve also has been called the ***Amelita Galla Curci*** or "high note" nerve after the opera singer. Injury to this nerve leads to inability to tense the ipsilateral vocal cord and hence difficulty "hitting high notes," projecting the voice, and voice fatigue during prolonged speech.

Histology

The thyroid gland is surrounded by the thyroid capsule, which is a thin layer of connective tissue. From the capsule, several septa extend within the thyroid parenchyma, which is subdivided into several lobules. The thyroid is divided into lobules that contain 20 to 40 follicles. There are roughly 3×10^6 follicles in the adult male thyroid gland. The follicles are spherical and average 30 µm in diameter. Epithelial cells (cuboidal or squamous) form the thyroid follicles; they are separated by thin connective stroma which is rich in both lymphatic and blood vessels. Small bundles of nerves are present. There is a colloidal gelatinous collection in the center of the follicle. Each follicle has two types of cells: follicular and parafollicular, or C cells. The follicular cells are responsible for the following actions: synthesis of thyroglobulin, iodination, storage of thyroglobulin, resorption of thyroglobulin, hydrolysis of thyroglobulin, and release of thyroid hormone into the blood and lymphatics.

PHYSIOLOGY

Iodine Metabolism

The average daily iodine requirement is 0.1 mg, which can be derived from foods such as fish, milk, and eggs, or as additives in bread or salt. In the stomach and jejunum, iodine is rapidly converted to iodide and absorbed into the bloodstream, from where it is distributed uniformly throughout the extracellular space. Iodide is actively transported into the thyroid follicular cells by an ATP-dependent process. In fact, the thyroid is the storage site of greater than 90% of the body's iodine content and accounts for one-third of the plasma iodine loss. The remaining plasma iodine is cleared via renal excretion

Thyroid Hormone Synthesis, Secretion, and Transport

The synthesis of thyroid hormone consists of several steps. The first step, iodide trapping, involves active (ATP-dependent) transport of iodide across the basement membrane of the thyrocyte via an intrinsic membrane protein, the Na^+/I^- symporter (NIS). Thyroglobulin (Tg) is a large (660-kDa) glycoprotein, which is present in thyroid follicles and has four tyrosyl residues. The second step in thyroid hormone synthesis involves oxidation of iodide to iodine and iodination of tyrosine residues on Tg, to form monoiodotyrosines (MITs) and diiodotyrosines (DITs). Both processes are

catalyzed by thyroid peroxidase. The recently identified protein pendrin is thought to mediate iodine efflux at the apical membrane. The third step leads to coupling of two DIT molecules to form tetraiodothyronine or thyroxine (T_4), and one DIT molecule with one MIT molecule to form 3,5,3'-triiodothyronine (T_3) or reverse 3,3',5'-triiodothyronine (rT_3). When stimulated by TSH, thyrocytes form pseudopodia that encircle portions of cell membrane containing thyroglobulin, which, in turn, fuse with enzyme-containing lysosomes. In the fourth step, thyroglobulin is hydrolyzed to release free iodothyronines (T_3 and T_4) and mono- and diiodotyrosines. The latter are deiodinated in the fifth step to yield iodide, which is reused in the thyrocyte.

Comparison of T_3 and T_4

	T_3	**T_4**
Production rate (nmol/day)	50	110
Fraction from thyroid	0.2	1.0
Relative metabolic potency	1.0	0.3
Serum concentration		
Total (nmol/L)	1.8	100
Free (pmol/L)	5	20
Fraction of total hormone in free form ($\times 10^{-2}$)	0.3	0.02
Distribution volume (L)	40	10
Fraction intracellular	0.64	0.15
Half-life (days)	0.75	6.7

KEY STEPS IN SYNTHESIS OF THYROID HORMONE

1. Active uptake of iodide (I^-) in exchange for Na^+.

2. Iodide may be discharged from the follicular cell by administration of competing ions such as perchlorate, bromide or chlorate.

3. Iodide uptake, the main control point for hormone synthesis, is stimulated by TSH.

4. Oxidation of iodide by hydrogen peroxide (H_2O_2) to form active iodine.

The reaction is catalyzed by thyroid peroxidase (TPO).

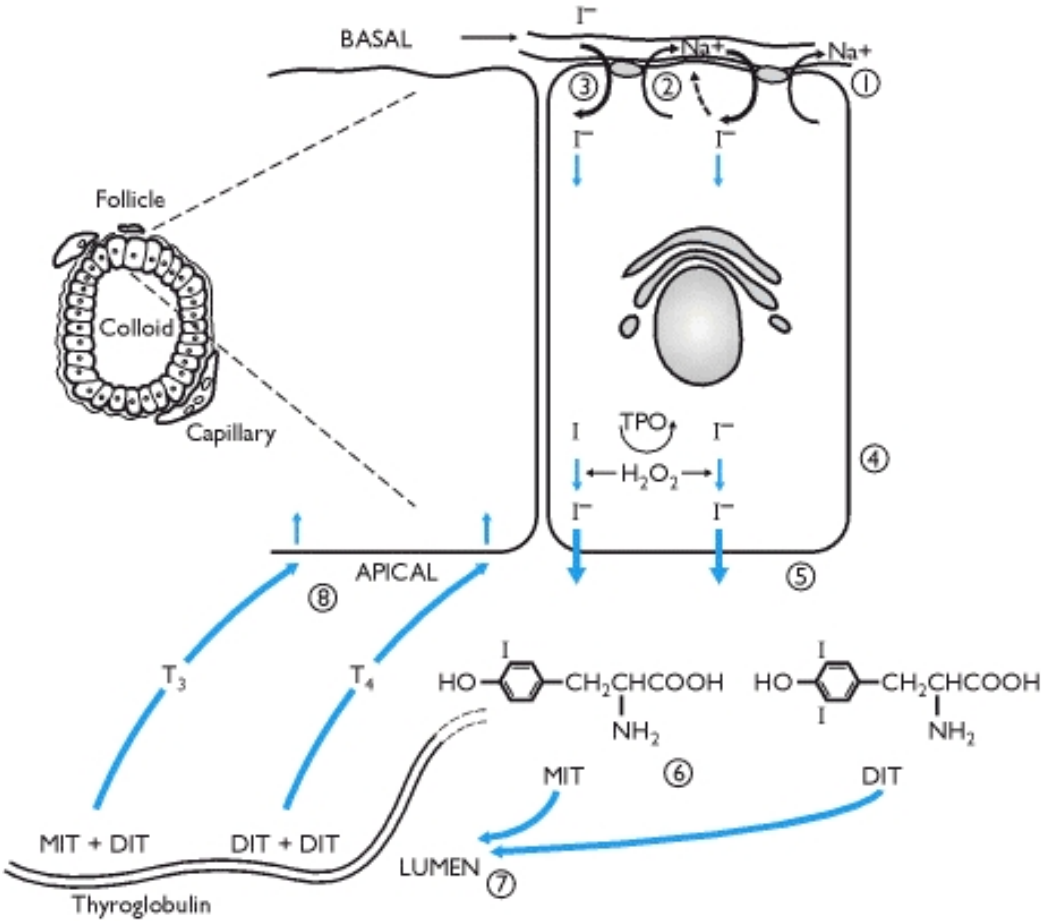
5. Active transport of iodine across the apical surface of the follicular cell.

6. Incorporation of active iodine into the tyrosine residues of thyroglobulin molecules to form mono- and di-iodotyrosines (MIT and DIT).

7. Uptake of the thyroglobulin into the lumen of the follicle and lining of iodinated tyrosine residues.

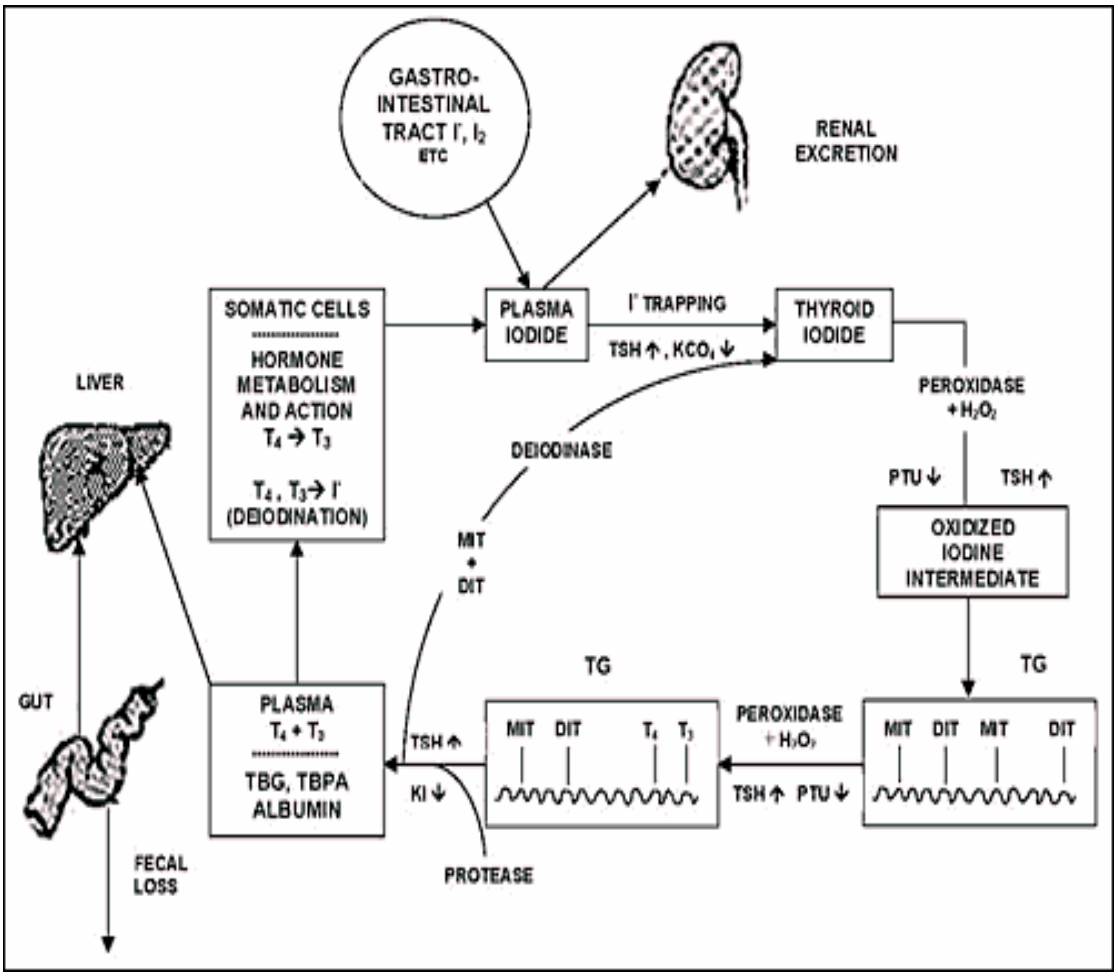
8. About 1% of stored colloid is removed each day. When the gland is very active this may rise to nearly 100% and colloid stores are depleted.

KEY STEPS IN SYNTHESIS OF THYROID HORMONE



SCHEMATIC REPRESENTATION OF THYROID HORMONE

SYNTHESIS AND RELEASE

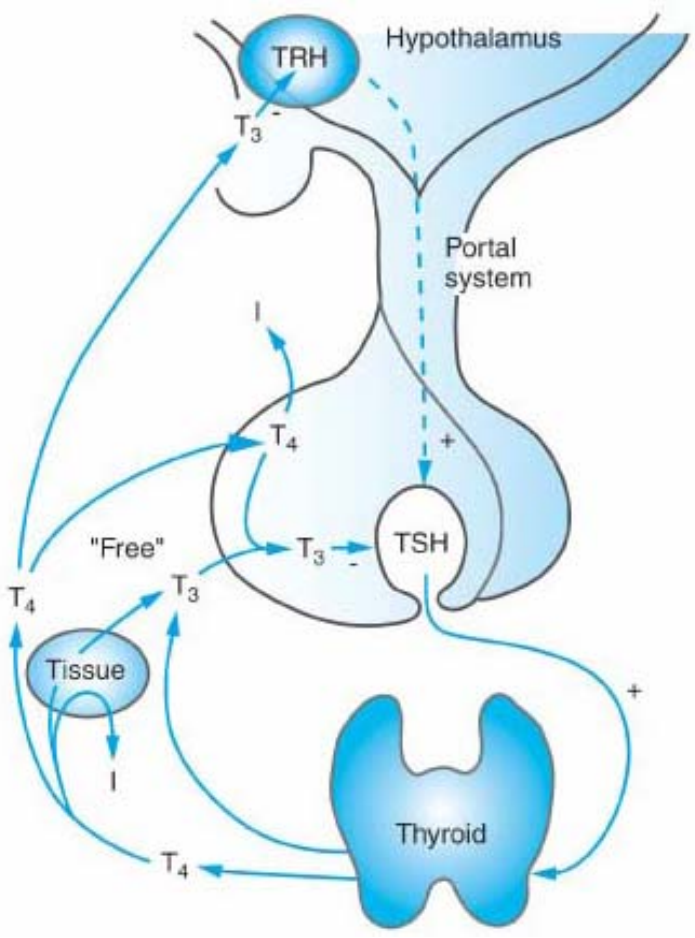


PHYSIOLOGICAL EFFECTS OF THYROID HORMONES

Target Tissue	Effect	Mechanism
Heart	Chronotropic	Increase number of β-adrenergic receptors.
	Inotropic	Enhance responses to circulating catecholamines.
		Increase proportion of α-myosin heavy chain (with higher ATPase activity).
Adipose tissue	Catabolic	Stimulate lipolysis.
Muscle	Catabolic	Increase protein breakdown.
Bone	Developmental	Promote normal growth and skeletal development.
Nervous system	Developmental	Promote normal brain development.
Gut	Metabolic	Increase rate of carbohydrate absorption.
Lipoprotein	Metabolic	Stimulate formation of LDL receptors.
Other	Calorigenic	Stimulate oxygen consumption by metabolically active tissues (exceptions: testes, uterus, lymph nodes, spleen, and anterior pituitary).
		Increase metabolic rate.

PITUITARY THYROID AXIS

Synthesis & liberation of thyroid hormones is controlled by TSH from anterior pituitary. Secretion of TSH depends on the level of circulating thyroid hormones in a classical negative feed back manner. Regulation of TSH secretion also results from the action of thyrotropin releasing hormone (TRH) produced in hypothalamus.



PATHOLOGY

A single palpable nodule in otherwise impalpable thyroid gland is called solitary nodule thyroid. A single discrete nodule in a palpable thyroid gland is called dominant nodule. Hence, the majority of thyroid nodules are benign and do not require removal. Therefore, it is of utmost importance to determine which patients with solitary thyroid nodule would benefit from surgery.

FORMATION OF NODULES

A loss of co-ordination between iodine metabolism, epithelial multiplication, thyroglobulin synthesis and colloid endocytosis are important in the genesis of nodule. Iodine deficiency and ingestion of goitrogens are the commonest cause of goitre formation. Iodine deficiency or goitrogens or hereditary factors lead to decrease in serum thyroid hormones with followed by increase in TSH which will produce diffuse hyperplastic goitre. The patient will become euthyroid because of normal thyroid hormone level, TSH level drops down and goitre disappears. If it persists after that it is a colloid goitre with inactive follicles. Because of fluctuation in TSH level, and varied response of cells to TSH, mixed active

and inactive follicles are formed. In active follicles, because of high vascularity, haemorrhage occurs with central necrosis. Growth stimulating antibodies are also responsible for multinodular goitre. Patient is usually euthyroid. Firm painless nodules are palpable; hardness may be due to calcification. Pain & sudden increase in size may be due to haemorrhage and simulate malignancy. Many thyroid disorders, both benign & malignant may manifest as solitary nodule.

CAUSES OF SOLITARY NODULE

A. CYST

Simple

Mixed – cystic and solid or complex

B.PALPABLE NODULE OF TRUE MULTINODULAR GOITRE

C.THYROIDITIS

Hashimoto’s thyroiditis

Sub-acute

D.INFECTION

Granulomatous disease

Abscess

E.ADENOMA

F.TOXIC ADENOMA

G. MALIGNANCY

Carcinoma – primary Differentiated

Papillay

Follicular

Medullary thyroid carcinoma

Undifferentiated

Anaplastic

- metastatic

Lymphoma

Clinically palpable nodule of a multinodular goitre is the most common cause of solitary nodule thyroid.

ADENOMA

Virtually all adenomas of thyroid present as a small discrete solitary nodule. They occur most commonly in young and middle aged women. They rarely exceed 3 cm. Almost all adenomas are of follicular variety. Rare types are papillary cystadenoma and Hurthle cell adenoma. The differentiation of a nodule within a multinodular goitre from an adenoma is difficult not only clinically but also anatomically.

The morphologic criteria used to identify adenoma are: complete fibrous encapsulation, a clear distinction between the architecture inside and outside the capsule, compression of thyroid parenchyma around the adenoma, lack of multinodularity in the remaining gland.

HISTOLOGICAL CLASSIFICATION OF ADENOMA

TYPE-I

A.EMBRYONAL ADENOMA

The follicles are premature, very cellular & arranged in the form of cords.

B. FETAL ADENOMA

Small follicles are arranged closely packed with an abundant connective tissue stroma.

C. SIMPLE ADENOMA

Composed of closely packed follicles of normal size.

D. COLLOID ADENOMA

Contains dilated follicles filled with colloid.

E. HURTHLE CELL ADENOMA

Composed of large granular cells identical to those encountered in various non – neoplastic thyroid lesions usually arranged in trabecular pattern.

Type II

A. Mircofollicular

B. Macrofollicular

C. Atypical adenoma

Exhibits nuclear atypia, variability in cell morphology, including the presence of spindle shaped cells.

Follicular adenomas are differentiated from follicular carcinoma by the absence of capsular or vascular invasion. Thus careful sampling of capsule is required to exclude carcinoma.

Adenomas attain certain size and remain in that because the expansile pressure restricts blood supply. It may suddenly enlarge and may be painful because of haemorrhage within the nodule. Adenomas occasionally have some dependence on TSH, so it regressed after administration of thyroid hormones.

Adenomatous goitre

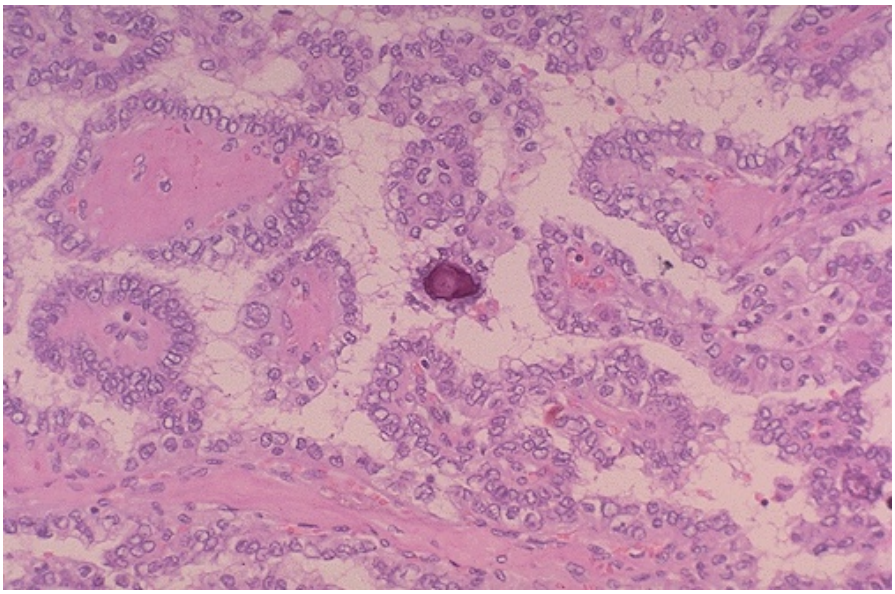
Adenomatous goitre is usually multinodular but a few may present as solitary nodule. Most patients are euthyroid. Whether single or numerous, adenomatous nodules have similar appearances.

Typical features include

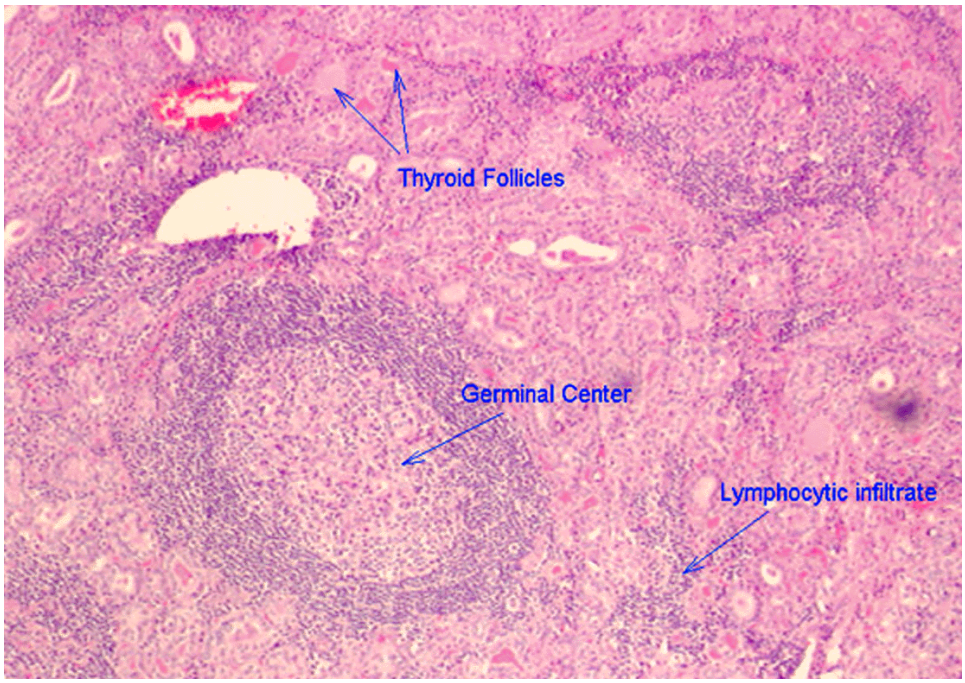
1. Nodularity created by islands of colloid filled or hyperplastic follicles.
2. Random irregular scarring.
3. Focal haemorrhages and haemosiderin deposition.
4. Focal calcification in areas of scarring
5. Microcyst formation.

Microscopically adenomatous nodules are composed of follicles of varying size. Some follicles are distended with colloid and lined by

PAPILLARY CARCINOMA



HASHIMOTO'S THYROIDITIS 1



flattened epithelium, whereas as other are small and are more active appearing.

CARCINOMA

Papillary Carcinoma: (70%)

Common in adults and children. Responsible for 30% of the thyroid carcinoma occurring below 40 yrs. More common in women. It grows slowly. Metastases to cervical lymph nodes are common. About 10-20% may present as only cervical lymph node metastases. The primary is occult (lateral aberrant thyroid). All the lesions below 1.0 cm are called as occult or micro carcinoma. Blood spread is unusual. Prognosis is good. 10 years survival rate is about 70– 80%.

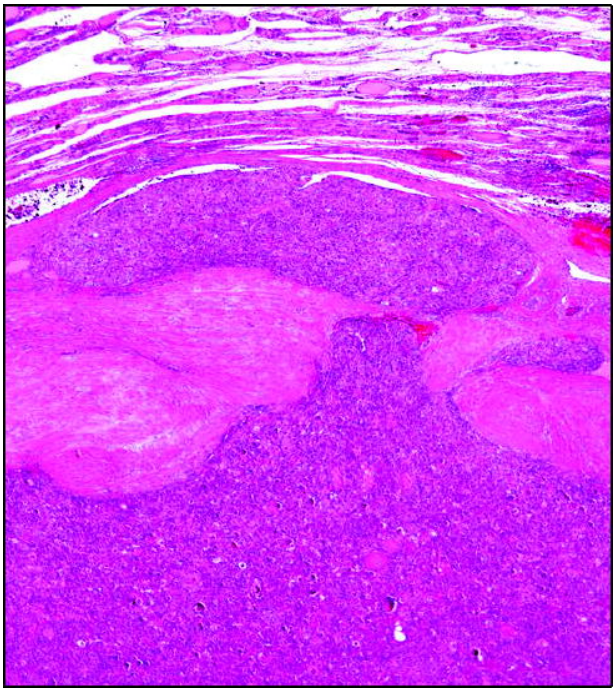
Histology

Complicated branching tree like pattern of cells outlined by papilliferous axial fibrovascular stroma. Pale, empty nuclei (Orphan Annie eyed nuclei) and Psammoma bodies are present. Papillary carcinoma is subjected to the influence of pituitary T.S.H.

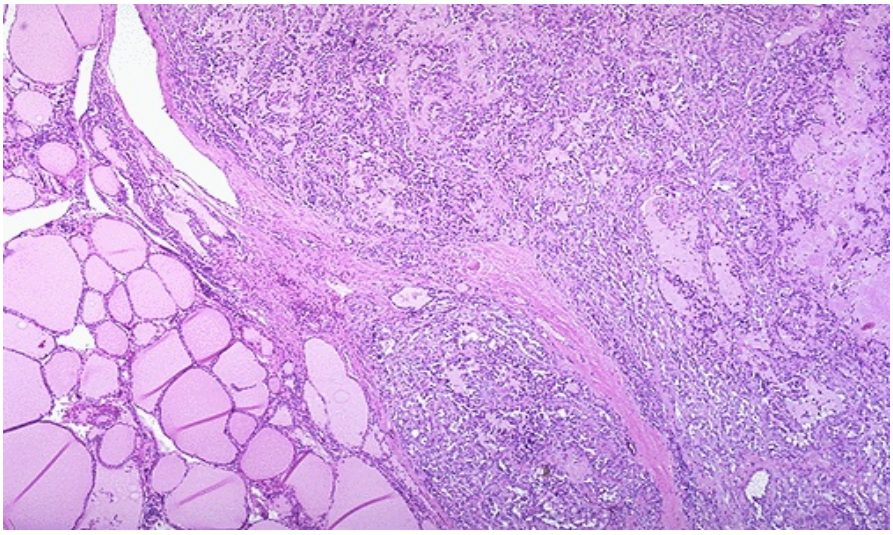
Follicular carcinoma (25%)

It is a well differentiated carcinoma of the thyroid but more aggressive than papillary carcinoma. More common in women. Peak incidence occurs in 5^{th} and 6^{th} decade.

FOLLICULAR CARCINOMA



MEDULLARY CARCINOMA



Two types:

i) Encapsulated - Less common

ii) Invasive mass

Haemorrhages, cystic degeneration and necrosis are common. Microscopically picture is that of adenocarcinoma with considerable range in size and differentiation of glands. Blood spread occurs in 70% cases. Commonest sites are lungs, bones, brain etc. Regional lymph nodes are involved in only 5% of cases.

Medullary carcinoma

Derived from parafollicular cells (C cells). It is an APUDOMA. 80% occur sporadically usually in adults. 10-20% occurs in children and teenagers with associated syndromes.

MEN IIa : MTC, Phaechromocytomas, parathyroid tumours.

MEN IIb : MTC, Phaechromocytomas + Mucosal neuroma, Marfanoid features, ganglioneuromatosis.

90% of the patients secrete calcitonin. Less frequently histamine, prostaglandins, ACTH and serotonin are secreted. It may present as a single nodule or multiple nodules. Sporadic forms occur in 5^{th} – 6^{th} decades. Often present in advanced forms. Familial type presents in second decade. Associated endocrine abnormalities bring the patient early. Diarrhoeas is

present in up to 30% of patients. Metastasis is usually to regional nodes (50%), lung, liver and bone. Medullary carcinoma is not TSH dependent. It does not take up radio iodine. Diagnosis of medullary carcinoma can be made by stimulating calcitonin secretion by Pentagastrin and calcium infusions.

Anaplastic carcinoma

Usually occurs in 7^{th} and 8^{th} decades of life, it is a rapidly growing, locally infiltrative tumour with very poor prognosis. It spreads by lymphatics and by blood stream. Two histological types are small cell carcinoma and giant cell carcinoma. I year survival is about 20%. Other tumours like lymphoma, sarcoma and secondaries also occur in thyroid. Secondary tumours usually arise from kidney, breast, colon, melanomas.

Thyroiditis

(i) Hashimoto's Thyroditis

It is an autoimmune thyroiditis. It is the commonest cause for goitrous hypothyroidism in places where iodine intake is adequate. It is a major cause for nonendemic goitre in children. The goitre is due to thyroid growth immunoglobulins like auto antibodies to thyrotrophin receptors, follicular microsomes, and thyroglobulin. Thyroid parenchyma is replaced by fibrous tissue because of the infiltration by lymphoid cells. So eventually hypothyroidism develops. Sometimes in the midcourse patient

may develop thyrotoxicosis called 'Hashitoxicosis'. More common in women at menopausal age. Usually both the lobes are involved. Nevertheless one lobe is larger than the other. It is lobulated and rubbery in consistency. It may be associated with pernicious anaemia, vitiligo, and Rheumatoid arthritis etc.

Histology

Excessive replacement of parenchyma by lymphocytes, plasma cells, macrophages, lymphoid germinal centers. Follicular cells are transformed into eosinophilic granular cystoplasmic cells called Hurthle cells (or oncocytes or Askanazy cells). Diagnosis rests on measurement of serum auto antibodies by Radio Immuno Assay. It is positive in over 85% of cases. Lymphoma may develop in Hashimoto's thyroiditis.

(ii) Subacute Thyroditis (De Quervain's Thyroiditis)

Causative agent is a virus, probably mumps virus. Patient has flu like illness followed by pain and rapid onset of swelling of thyroid. Swelling may be diffuse or asymmetrical, and tender on palpation. During active phase patient may develop hyperthyroidism, then due to extensive destruction hypothyroidism develops.

Histology:

Aggregation of macrophages admixed with multi nucleated giant cells. It is a self limiting condition. Acute bacterial thyroiditis is rare. Commonest organisms are staphylococcus.

(III) **Riedel's Thyroiditis (Ligneous Thyroiditis).**

Aetiology is unknown. There is extensive fibrosing reaction that destroys more or less all the thyroid gland. The fibrous tissue may extend beyond the capsule and involve other structures in the neck. More common in females. It is characterized by painless enlargement of thyroid, woody hard in consistency, asymmetrical, pressure symptoms may be present especially tracheal compression. It may be associated with retroperitoneal fibrosis. Occasionally it may be associated with sclerosing cholangitis. About 25-50% of the patients are hypothyroid.

Toxic Adenoma:

This type produces hormones in sufficient quantity to give rise to hyperthyroidism. Thyroxine output is not controlled by TSH or LATS. It is an autonomous tumour. Patient has increased metabolic rate, loss of weight, intolerance to heat, tremors, and fibrillations. Usually there is no exophthalmos. Radioiodine scan shows it to be a hot nodule.

CLINICAL PRESENTATION

Patients with solitary nodule in thyroid may present for:

- Toxic symptoms (autonomous, hyper functioning nodule).
- Pressure symptoms – dyspnoea, dysphagia, hoarseness of voice and rarely superior venacaval obstruction.
- Metastatic disease in the neck lymph nodes
- Distant metastasis.
- Cosmetic reasons.

CLINICAL RISK FACTORS

Age

The risk of cancer in a solitary thyroid nodule is more than 10% in adults. This risk is more in teenagers and after 60 years of age (30% - 40%).

Sex

Nodules in men are more likely to harbour malignancy than in women.

Growth Patterns

A nodule that has appeared recently or one that has undergone progressive enlargement over months is suspicious of malignancy.

A CASE OF FOLLICULAR ADENOMA

However sudden painful enlargement of a nodule is usually due to haemorrhage with in the nodule.

IRRADIATION

The finding of solitary thyroid nodule in an individual with a history of external irradiation therapy over face, neck and chest should be regarded with a high degree of suspicion for the presence of malignancy.

FAMILY HISTORY

The presence of a solitary nodule in a patient with a family history of thyroid malignancy increases the risk for malignancy in the nodule.

PHYSICAL CHARACTERISTICS OF THYROID NODULE

1. **Single versus multiple:**

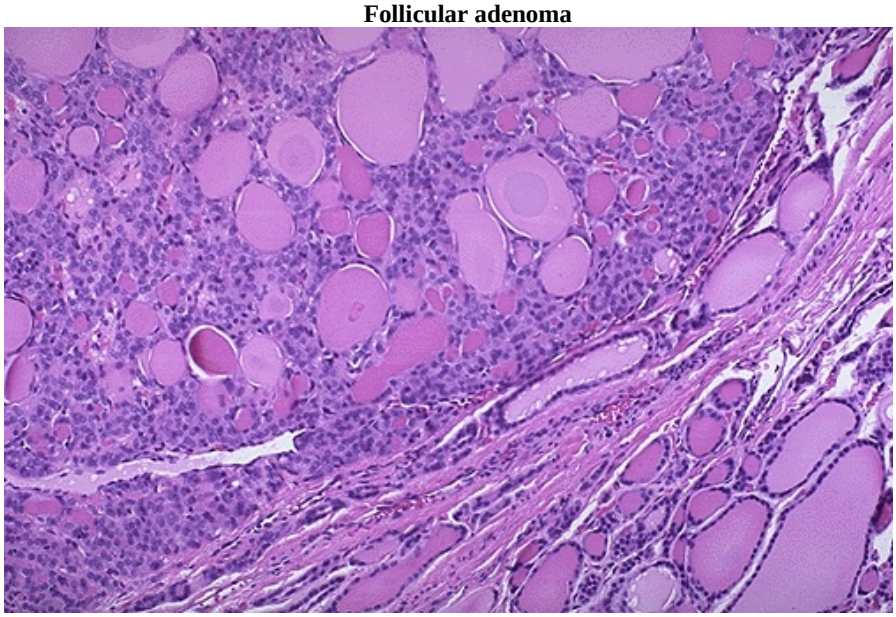
   Malignancy occurs in 10-20% of single thyroid nodules but in only 3-5% multinodular goitre.

2. **Consistency and fixation:**

   Hard consistency and the clinical impression of fixation implying invasion of adjacent structures also suggest malignancy. Indeed the majority of cancers occurring in single nodules are mobile and indistinguishable from benign lesions.

Solitary nodule thyroid

Follicular adenoma



3. Recurrent nerve paralysis.

In the absence of previous neck surgery, it is virtually pathognomonic of malignancy.

4. Obstructive signs:

Clinical evidence of obstruction of the airway or of the great veins of neck and mediastinum by a solitary thyroid nodule is rare, but when present, should raise the suspicion of malignancy.

5. Lymph nodes

Associated palpable cervical lymph adenopathy points strongly to cancer

6. Distant metastasis.

CLINICOPATHOLOGICAL STAGING OF THYROID CARCINOMA; (DEGROOT)

I. A. Unilateral confined to thyroid

B. Bilateral or multifocal

II. A. Unilateral Significant cervical nodes

B. Bilateral cervical or mediastinal lymph nodes

III. Local invasion with or without positive nodes

IV. Distant metastasis

TNM classification is separate for each type of thyroid carcinoma.

MULTINODULAR GOITRE

Definitions of low risk and high risk for differentiated carcinoma as per lahey clinic.

* AGES Scale : Age, Grade of Tumour, Extent of disease, Size of tumor
* MACIS Scale : Metastases: Age, extent of Clearance, Invasion,

  Size of tumour.
* AMES Scale : Age, Metastases, Extent of invasion, Size of tumour.
* Men of 40 years and younger, women of 50 years and younger without distant metastases.
* All older patients with intra thyroid papillary carcinoma of follicular carcinoma with minor capsular involvement, in association with tumors less than 5 cm in diameter and no distant metastases.

High risk group:

- All patients with distant metastases
- All older patients with extra thyroid papillary carcinoma or follicular carcinoma with major capsular involvement and tumors 5 cm in diameter or larger regardless of extent of disease.

TNM STAGING

Primary tumor

TX: Primary tumor cannot be assessed

T0: No evidence of primary tumor

T1: The tumor is 2 cm or less in diameter

T2: Tumor is between 2 cm and 4 cm across

T3: Tumor is larger than 4 cm limited to thyroid or with extrathyroidal extension

T4a: Tumor of any size and has grown extensively beyond the thyroid capsule to invade soft tissues, larynx,trachea, esophagus RLN

T4b: Tumor invades prevertebral fascia,encases carotid artery /mediastinal vessels

For anaplastic thyroid cancers:

T4a: Tumor is still within the thyroid and may be resectable

T4b: Tumor has grown outside of the thyroid and is not resectable

Regional lymph Nodes

NX: Regional (nearby) lymph nodes cannot be assessed

N0: No regional lymph nodes spread

N1: Spread to regional nodes present

N1a: Metastases to level VI (cervical)

N1b: Metastases to unilateral bilateral or contralateral neck or the upper mediastinal nodes

Distant Metastases:

MX: Presence of distant metastasis (spread) cannot be assessed

M0: No distant metastasis

M1: Distant metastasis is present

STAGE GROUPING	
Papillary or Follicular Tumors	
Stage	**TNM**
Younger than age 45 Years	
I	Any T, Any N, M0
II	Any T, Any N, M1
Age 45 Years and older	
I	T1, N0, M0
II	T2, N0, M0
III	T3, N0, M0; T1-3, N1a, M0
IVA	T4a, N0-1a, M0; T1-4a, N1b, M0
IVB	T4b, Any N, M0
IVC	Any T, any N, M1
Medullary Thyroid Cancer	
Stage	**TNM**
I	T1, N0, M0
II	T2-3, N0, M0
III	T1-3, N1a, M0
IVA	T4a, N0-1a, M0; T1-4a, N1b, M0
IVB	T4b, any N, M0
IVC	Any T, Any N, M1
Anaplastic Cancer	
Stage	**TNM**
IVA	T4a, Any N, M0
IVB	T4b, Any N, M0
IVC	Any T, Any M, M1

Evaluation of Patients with Thyroid Disease

Tests of Thyroid Function

Serum TSH: The tests for serum TSH (normal 0.5 to 5 μU/mL) are based on the principle that monoclonal TSH antibodies are bound to a solid matrix and bind serum TSH. The amount of serum TSH is proportional to the amount of bound secondary antibody (immunometric assay). Older radioimmunoassays for TSH were able to detect elevated TSH levels in hypothyroidism, but were not sensitive enough to detect suppressed levels of TSH characteristic of hyperthyroidism. Newer, second-generation, "sensitive" TSH assays can measure levels less than 0.1 μU/mL and third-generation or "supersensitive or ultrasensitive" assays can detect TSH levels as low as 0.01 μU/mL. Serum TSH levels reflect the ability of the anterior pituitary to detect free T_4 levels. There is an inverse relationship between the free T_4 level and the logarithm of the TSH concentration—small changes in free T_4 lead to a large shift in TSH levels. Thus, the ultrasensitive TSH assay has become the most sensitive and specific test for the diagnosis of hyper- and hypothyroidism and for optimizing T_4 replacement and suppressive therapy.

Total T_4 and Total T_3: Total T_4 (reference range: 55 to 150 nmol/L) and T_3 (reference range: 1.5 to 3.5 nmol/L) levels are measured by radioimmunoassay and measure both the free and bound components of the

hormones. Total T_4 levels reflect the output from the thyroid gland, whereas T_3 levels in the non-stimulated thyroid gland are more indicative of peripheral thyroid hormone metabolism and are, therefore, not generally suitable as a general screening test. Total T_4 levels are increased not only in hyperthyroid patients, but also in those patients with elevated thyroglobulin levels secondary to pregnancy, estrogen/progesterone use, or congenital diseases. Similarly, total T_4 levels decrease in hypothyroidism and in patients with decreased thyroglobulin levels caused by anabolic steroid use and by protein-losing disorders such as nephrotic syndrome. Individuals with these latter disorders may be euthyroid if their free T_4 levels are normal. Measurement of total T_3 levels is important in clinically hyperthyroid patients with normal T_4 levels, who may have T_3 thyrotoxicosis. As discussed previously, total T_3 levels are often increased in early hypothyroidism.

Free T_4 and Free T_3: These radioimmunoassay-based tests are a sensitive and accurate measurement of biologically active thyroid hormone. Free T_4 (reference range: 12 to 28 pmol/L) estimates are not performed as a routine screening tool in thyroid disease. Use of this test is confined to cases of early hyperthyroidism in which total T_4 levels may be normal but free T_4 levels are raised. In patients with end-organ resistance to T_4 (Refetoff syndrome), T_4 levels are increased, but TSH levels usually are normal. Free

T_3 (reference range: 3 to 9 pmol/L) is most useful in confirming the diagnosis of early hyperthyroidism, in which levels of free T_4 and free T_3 rise before total T_4 and T_3. Free T_4 levels may also be measured indirectly using the T_3 resin-uptake test. If free T_4 levels are increased, fewer hormone-binding sites are available for binding radiolabeled T_3 that has been added to the patient's serum. Therefore, more T_3 binds with an ion-exchange resin and the T_3 resin uptake is increased.

Thyrotropin-Releasing Hormone : This test is useful to evaluate pituitary TSH secretory function and is performed by administering 500 µg of TRH intravenously and measuring TSH levels after 30 and 60 minutes. In a normal individual, TSH levels should increase at least 6 µIU/mL from the baseline.

Thyroid Antibodies: Thyroid antibodies include antithyroglobulin (anti-Tg), antimicrosomal or antithyroid peroxidase (anti-TPO) and thyroid-stimulating immunoglobulin (TSI). Anti-Tg and anti-TPO antibody levels do not determine thyroid function; instead, they indicate the underlying disorder, usually an autoimmune thyroiditis. Approximately 80% of patients with Hashimoto's thyroiditis have elevated thyroid antibody levels, but levels may also be increased in patients with Graves' disease, multinodular goiter, and, occasionally, with thyroid neoplasms.

Serum Thyroglobulin: Thyroglobulin is increased dramatically in destructive processes of the thyroid gland, such as thyroiditis or overactive states such as Graves' disease and toxic multinodular goiter. Used in monitoring patients with differentiated thyroid cancer for recurrence, particularly after total thyroidectomy and radioactive iodine ablation.

Thyroid Imaging

Radionuclide Imaging

Both iodine-123 (^{123}I) and iodine-131 (^{131}I) are used to image the thyroid gland. The former emits low-dose radiation, has a half-life of 12 to 14 hours, and is used to image lingual thyroids or goitres. In contrast, ^{131}I use leads to higher-dose radiation exposure and has a half-life of 8 to 10 days. Therefore, this isotope is used to screen and treat patients with differentiated thyroid cancers for metastatic disease. The images provide information about the size shape of the gland, distribution of functional activity. Areas that trap less radioactivity than the surrounding gland are termed "cold" , whereas areas that demonstrate increased activity are termed "hot." The risk of malignancy is higher in "cold" lesions (15 to 20%) than in "hot" or "warm" lesions (<5%). Technetium-99m (^{99m}Tc) pertechnetate is taken up by the thyroid gland and also used for thyroid evaluation. This isotope is taken up by the mitochondria, but is not organified. It also has the advantage of having a shorter half-life and minimizes radiation exposure. It

is particularly sensitive for nodal metastases. More recently, 18 F-fluorodeoxyglucose positron emission tomography (FDG PET) has been used to screen for metastases in patients with thyroid cancer, in whom other imaging studies are negative. However, this technique is expensive and not widely available.

Ultrasound

Excellent, noninvasive and portable imaging method and it has the added advantage of no radiation exposure. It is helpful in the evaluation of thyroid nodules, distinguishing solid from cystic ones, and providing information about size and multicentricity. Assess cervical lymphadenopathy, guide fine-needle aspiration (FNA) biopsy. However, it cannot be used to image thyroid tissue outside the neck (e.g., to assess the extent of a substernal goiter).

CT/MRI Scan

Provide excellent imaging of the thyroid gland and adjacent nodes, and are particularly useful in evaluating the extent of large, fixed or substernal goiters and their relationship to the airway and vascular structures. Noncontrast CT scans should be obtained in patients who are likely to require subsequent radioactive iodine therapy.

FNAC

The investigation of choice for discrete thyroid swellings. Excellent patient compliance, simple, quick to perform in OP department. USG guided aspiration achieves more accurate sampling and reduces unsatisfactory aspirates. There are few false positive with respect to malignancy but definite false negative rate with respect to both benign and malignant nodules.

Its use in the recent years has resulted in a significant decrease in the number of thyroid surgeries being performed, while increasing the yield of malignant lesions of patients who have undergone surgery.

CLASSIFICATION OF FNAC REPORTS:

THY1 NON DIAGNOSTIC

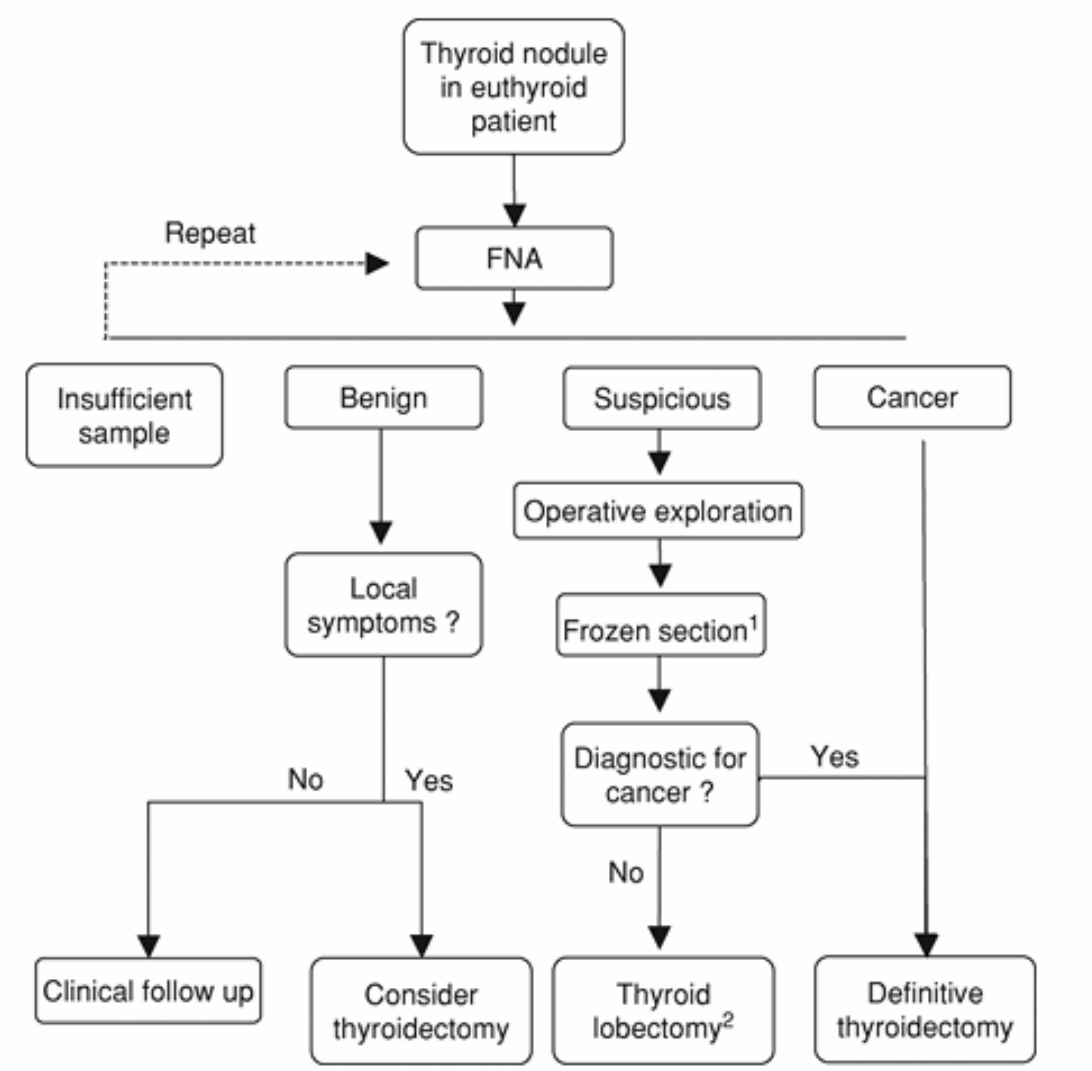
THY2 NON NEOPLASTIC

THY3 FOLLICULAR

THY4 SUSPICIOUS OF MALIGNANCY

THY5 MALIGNANT

Flow diagram for the evaluation of thyroid nodule based on the results of fine needle aspiration biopsy



[1] Consider touch preparation.[2] Consider total thyroidectomy for large, nodular, and/or bilateral lesion, as well as in patients with a history of radiation exposure in childhood.

MANAGEMENT

Management opted for solitary thyroid nodules are

1. Surgical
2. Non-Surgical

SURGICAL

Advised after cytological impression

Indications:

1. All proven malignant nodules
2. All cytologically diagnosed follicular neoplasm
3. All lesions exhibiting an atypical pattern but non-diagnostic cellular pattern on cytology.
4. All papillary adenomas
5. Cystic lesion which recurred following aspiration; > 4 cm in size; complex in nature.
6. High suspicion of malignancy on clinical grounds even if cytology suggests benign disease and presence of high – risk factors.
7. Hyper functioning nodule resulting hyperthyroidism.
8. Obstructive symptoms, actual or potential Patient anxiety
9. Patient anxiety
10. Cosmesis.

The standard surgical procedure in a benign single nodule should be Hemithyroidectomy. The line of resection should be extended to the junction of the isthmus & the contralateral lobe.

Patients with toxic nodule may be treated by surgery. Ideal procedure is Hemithyroidectomy. Prior to surgery patient should be brought to euthyroid state with propranolol and carbimazole. Surgical treatment is safe, certain and without morbidity. Patients with toxic nodule over the age of 45 years can be treated with radioiodine.

In patients with differentiated thyroid carcinoma, there are two schools of thought,

1. HEMI THYROIDECTOMY
2. TOTAL OR NEAR TOTAL THYROIDECTOMY

The Treatment objectives in differentiated thyroid cancer are

1. Eradicate primary disease
2. Reduce the incidence of local / distant recurrence
3. Facilitate the treatment of metastasis.
4. Cure the maximum number of patients.
5. Achieve all of the above with minimal morbidity.

In case of micro-papillary carcinoma, and minimally invasive follicular carcinoma and the rare encapsulated papillary carcinoma, hemi thyroidectomy is the treatment. In all other cases of differentiated thyroid cancers total thyroidectomy is the procedure of choice.

There are several arguments for treatment of differentiated thyroid cancer by total / near total thyroidectomy.

i) Multifocal disease

ii) Decreased incidence of local recurrence

iii) Reduced risk of anaplasia in any residual tissue.

iv) Facilitation of diagnosing unsuspected metastatic disease by radioactive iodine scanning or treatment with I^{131}.

v) Greater sensitivity of blood thyroglobulin levels to predict persistent / recurrent disease.

If total thyroidectomy is contemplated, it is not better than near total thyroidectomy in which 1 - gms of normal thyroid tissue is preserved on the contralateral side to protect blood supply to one or more parathyroid glands.

If conservative surgery has been done TSH is suppressed by levothyroixine 0.2 – 0.3 mg/day. But TSH suppression is of doubtful value in Low risk patients.

In preparing patients for isotope scanning, T_4 is stopped 8 weeks before and T_3 is used for the first 6 weeks and stopped only 2 weeks before so that the patient will not develop thyroid insufficiency. A low iodine diet is also recommended during those 2 weeks.

If lymph nodes are affected by secondary deposits in cases of papillary carcinoma of MTC and if a nodule of MTC is > 2 cm in size, modified neck dissection is performed on the ipsilateral side. Routine central neck node dissection is done for Hurthle cell carcinoma and MTC and in cases of involved central nodes bilateral neck dissection should be done.

If distant metastases are found, they are treated with large doses of ^{131}l. The alternative is TSH suppression with T_3.

In patients with medullary carcinoma the treatment of choice is total thyroidectomy with central neck node dissection and T3 replacement therapy. Close relatives are screened by estimating serum calcitonin in both basal and after pentagastrin or calcium. If rise in serum calcitonin is observed, prophylactic thyroidectomy is done. Phaeochromocytoma should e excluded before surgery, Screening of family members with RET proto-oncogene point mutation has replaced the provocation tests.

In case of anaplastic carcinoma, total thyroidectomy with modified neck dissection is treatment of choice but in almost all patients it is not respectable. Isthmusectomy is done to decompress trachea and to obtain tissue for histology. External irradiation should be given in all cases for palliation of pain and dyspnoea. Chemotherapy with Adriamycin or Adriamycin, chlorambucil and vincristine combination area advised.

In case of lymphoma, radical surgery is unnecessary. Once the diagnosis is established by biopsy, Isthmusectomy is done for tracheal decompression. Lymphoma responds well to radio therapy.

THYROIDECTOMY PROCEDURE

For Hemi thyroidectomy

1. Patient in supine position, neck extended with the help of a sandbag placed between the shoulders and rotation of the head is avoided by keeping the head on a ring.
2. A transverse collar incision is made about two finger breadth above the clavicle.
3. Elevation of upper & lower flaps in the plane between platsyma and deep cervical fascia.
4. Vertically incise the deep cervical fascia in the midline.
5. Vertically split infrahyoid muscles.

6. Ligate and divide middle thyroid vein.
7. Ligate and divide superior thyroid pedicle
8. Inferior thyroid artery to be ligated in continuity away from the gland.
9. The thyroid isthmus is clamped at the junction with contralateral lobe and divided.

For total thyroidectomy:

The same technique to be followed on contralateral side also. The parathyroids are carefully separated and left insitu.

NON SURGICAL MANAGEMENT

Thyroid surgery, even in experienced hands, is associated with definite morbidity and should not be undertaken lightly. When the question of malignancy with a solitary thyroid nodule has been eliminated by FNAC and in the absence of obstructive symptom, it is reasonable to offer the patient a conservative line of management. Review the patient after 6 months, carry out a full cervical examination and repeat the FNAC. Provided there is no clinical suspicion of cancer and the cytology again is unequivocally benign, the individual is seen on a annual basis for re examination and further FNAC. Suppressive dose of exogenous T4 to inhibit further growth of solitary thyroid nodule is a controversial question.

MATERIALS and METHODS

MATERIALS AND METHODS

This is a prospective study of randomly selected patients with clinically palpable, solitary nodule thyroid diagnosed and treated at Kilpauk Medical College Hospital. Total duration of study was two years, from September 2006 to September 2008.

Each patient's symptoms and signs were entered in a proforma (given at the end of the dissertation) with clinical examination in relation to the thyroid swelling and lymph node involvement and a routine systemic and general examination was done.

All the patients were subjected to basic investigations like complete hemogram. Blood sugar, urea, serum cholesterol, urine analysis, chest radiogram and neck radiogram. Tissue diagnosis was obtained by fine needle aspiration cytology in all these patients.

Thyroid profile was done in selected patients with features of hyper or hypofunctioning of the gland. Radioiodine study was not done since the facility was not available at our hospital. Ultrasound of neck and Computed Tomogram scan of, chest and skull were done in selected patients. All operated specimens were subjected to histopathological examination.

Preoperative and postoperative complications were analysed. Most cases were regularly followed up throughout the study period. All the observations were analysed and compared with other studies.

OBSERVATION

OBSERVATION

PREVALENCE OF SOLITARY NODULE THYROID

TABLE : 1

NO OF THYROID CASES ADMITTED	SOLITARY THYROID NODULE	PERCENTAGE
390	80	20.51

Solitary nodule thyroid represents thyroid pathology in about 20.51% of case. Out of 80 patients 70 were females and 10 were males. This gives a Male: female ratio=1:6.solitary nodule thyroid is 6 times more common in women.

TABLE : 2

SEX DISTRIBUTION

SEX	MALE	FEMALE
Number of patients	10	70
Percentage	12.5%	87.5%

This distribution is in accordance with most of the reported series in our country and else where. Considering the total number of admission of any thyroid swelling the female incidence is more partly because of increased prevalence and partly because of increased cosmetic awareness among young females.

TABLE:3

AGE DISTRIBUTION

AGE IN YEARS	NO.OF PATIENTS	PERCENTAGE
UPTO 20	5	**6.25%**
21-30	25	**31.25%**
31-40	27	**33.75%**
41-50	11	**13.75%**
51-60	10	**12.50%**
ABOVE 60	2	**2.50%**

In this study the youngest patient was 16 years old and the oldest was 65 years old.80% of solitary nodules occurred during the age between 21-50 years. The highest incidence of 33.75 % was recorded during the 4th decade of life which is comparable with study done by B. Srinivas Pai, Vijai N. Anand, K. Rajgopal Shenoy

TABLE-4

SIDE OF INVOLVEMENT

SIDE	RIGHT	LEFT
No of patients	54	26
Percentage	68%	32%

TABLE-5

CLINICAL PRESENTATION

Clinical presentation	No of patients	Percentage
Swelling thyroid region	80	100%
Pain	6	7.5%
Toxic symptoms	3	3.75%
Dyspnoea	2	2.5%
Dysphagia	10	12.5%
Sudden increase in size	7	8.75%
Regional palpable lymphadenopathy	2	2.5%
Hoarseness of voice	1	1.25%
Hard consistency	4	5%

All the patients had only single palpable nodule. Toxic symptoms were present in 3 patients. Clinical evidence of obstruction to airway or of the great veins of neck by a solitary nodule thyroid is rare. Seven patients complained of sudden increase in size, while hoarseness of voice was present, only in 1 case. In this study, 2 patients had regional lymphadenopathy; which on FNAC proved to be secondary deposits from papillary carcinoma. 10 patients had difficulty in swallowing and 6 patients, pain over the swelling. 2 patients had difficulty in breathing, which was mostly uncharacteristic; neither exertional nor positional.

TABLE-6

HORMONAL STATUS (CLINICAL)

HORMONAL STATUS	TOTAL NO. OF PATIENTS	PERCENTAGE
Euthyroid	**77**	**96.25**
Hyperthyroid	**3**	**3.75**
Hypothyroid	**-**	**-**

DIAGNOSTIC WORKUP:

In this study the following investigations were done in all patients which included urine analysis, blood sugar, urea, and serum creatinine, plain radiograph of neck, IDL scopy, chest radiograph and fine needle aspiration cytology. USG and CT scan were done in few cases. Serum T3, T4 and TSH estimation were done. CT scan done in a patient with extensive neck secondaries. Radionucleotide scanning was not done for any patients due to the non-availability of the facility in our hospital. FNAC is the investigation of choice for solitary thyroid nodule. In this study FNAC was a very dependable and an easy investigation without complications.

TABLE-7

FNAC REPORT

SL .NO	FNAC REPORT	NO OF PATIENTS
1	FOLLICULAR NEOPLASM	**40**
2	NODULAR GOITRE	**31**
3	PAPILLARY CARCINOMA	**6**
4	HASHIMOTO'S THYROIDITIS	3
5	THYROID CYST	**-**

Amongst the FNAC reports, follicular neoplasm was the most common to be reported with the inability to identify vascular/capsular invasion. Adenomatous goitre, presenting as a solitary nodule was next commonest eventuality. 6 Cases were reported as papillary carcinomas with 2 of them showing deposits in neck nodes.

TABLE-8

MANAGEMENT DONE

SL.NO	**MANAGEMENT**	NO.OF PATIENTS
1	Hemithyroidectomy	64
2	Sub-total thyroidectomy	5
3	Near total-thyroidectomy	1
4	Total thyroidectomy with block dissection	2
5	Total thyroidectomy without block dissection	3
6	Conservative follow up	3
7	Not willing for surgery	2
	TOTAL	80

Out of 80 patients, 75 were submitted to surgery with below mentioned indications.2 patients were given conservative line of management because of IHD with very low ejection fraction. One another patient with Hashimoto's thyroiditis also was put on conservative treatment. 2 patients were not willing for surgery. These patients were advised regular follow up, on a half yearly basis for re-examinations and repeat FNAC. Repeat FNAC was done in 2 of these patients and were reported benign. Provided there is no clinical suspicion of cancer and the cytology is again unequivocally benign, the individuals are seen on an annual basis for re-examination and further FNAC (RUSSEL).

TABLE-9

INDICATIONS FOR SURGERY

SL.NO	INDICATIONS FOR SURGERY	NO.OF PATIENTS
1	Cytology proven malignancy	**6**
2	Cytology diagnosis as follicular neoplasm	**40**
3	Clinical suspicion of malignancy	**1**
4	Toxic nodule	**3**
5	Cosmetic	**25**
	Total	**75**

This study includes three cases of solitary thyroid nodule with hyperthyroidism with benign cytology report. For these patients Hemithyroidectomy was done after preparation with anti-thyroid drugs, on the assumption that the solitary nodule is the overactive tissue, since radioisotope scan was not available to study the functional status of the nodule and these patients had no recurrence thyrotoxicosis.

Total thyroidectomy was done for 5 patients of papillary carcinoma with functional neck node dissection in 2 patients. Near-total thyroidectomy was done for a patient with papillary carcinoma leaving behind a strip of tissue on the side other than the nodule.

Sub-total thyroidectomy was done for a 5 patients who had nodules on contralateral lobe peroperatively. Hemi-thyroidectomy, the

standard surgical procedure for solitary nodule thyroid was done in 64 patients i.e., about 84% of patients who underwent surgery. All resected specimens were submitted to histopathological examination.

TABLE-10

HISTOPATHOLOGICAL REPORT

HPE REPORT	NO. OF PATIENTS	PERCENTAGE
CARCINOMA:	**10**	**13.33%**
Papillary carcinoma and follicular variant of papillary carcinoma	**8**	
Follicular carcinoma	**2**	
Follicular adenoma	**36**	**48%**
Nodular goitre	**27**	**36%**
Hashimoto's thyroiditis	**2**	**2.67%**
Total	**75**	

Histology proven malignancy in this series of study of solitary thyroid nodule is 13.33% of which 80% (8 cases) were of papillary carcinoma and its variant and the rest 20% (2 cases) were follicular carcinoma types. Of these, six cases were diagnosed preoperatively and were offered the confirmative treatment the rest four cases were diagnosed only on HPE reporting & then underwent completion total thyroidectomy without neck dissection. All these patients are under regular follow up with suppressive doses of thyroxine.

DISCUSSION

DISCUSSION

The estimated life time risk of developing a nodule in the thyroid was projected to be between 5-10%, according to a prospective study conducted in Framingham, Massachusetts, in 1950s & 1960s. According to the study conducted by Prof .R.L. Gupta University College of medical science, Delhi right lobe involvement is more 51.4% compared to left lobe involvement of 38.8% which is comparable with our study with right lobe involving 68% and left lobe 32%.

In a study conducted in MKG medical college Berhrampur Orissa (1990-1998) under Prof. M.C.Dandapat, Dr. L.M.Mukarjee concluded that the maximum number of cases recorded during the 3^{rd} and 4^{th} decade of life with a female & male ratio of 5:1 which is comparable with our study which has a ratio of 6:1. Nagori et al reported the maximum incidence of SNG of 29% during the 4^{th} decade. The commonest site of SNG was right lobe. The percentage of malignancy was 11.1%. In a study Dr.H.Koticha & R.M.S Kamdar Mumbai concluded that, estimation of thyroid hormone levels has made no significant impact in deciding about surgery. FNAC is safe, simple diagnostic but surgery is mandatory.

After an analysis of 100 cases of thyroid nodules, Prof. R.C. Suryaprakash concluded that among the thyroid disorder adenoma thyroid was the commonest benign lesions, papillary carcinoma was the commonest

malignancy. Hashimoto's thyroiditis has got the highest incidence among the middle aged women.

Comparison of pre-operative FNAC with post-operative Histopathological examination:

Out of 75 cases operated 5 had different HPE reports as compared to FNAC reports. If both FNAC & HPE are benign or malignant they are considered as true positive.4 cytologically benign lesions were reported as malignant on HPE. So FNAC was false negative in these cases.

TABLE-11

ACCURACY RATE OF FNAC

RESULT	True positive cases	False negative	False positive	TOTAL
NO. OF CASES	71	4	0	75
PERCENTAGE	94.6%	5.3%	0	100

In comparison an overall accuracy rate greater than 94% was achieved in the cytological diagnosis of SNG. The main goal of FNAC is to accurately predict which nodule is cancerous. Numerous studies cited the following data.

Sensitivity is 65% to 100%, specificity is 70% to 100%. Overall accuracy rate is estimated to be 92-95%.in most series false positive rate is approximately 0.8% - 9% & the false negative rate is 0-16%. Most expertise agrees that the actual false negative rate is less than 5%.

CANCER RISK IN FOLLICULAR NEOPLASM

The cytological appearances of follicular adenoma and carcinoma are very similar. So a cytological diagnosis of follicular neoplasm is only possible, and confirmation of diagnosis of follicular carcinoma depends upon the visualization of capillary & capsular invasion in HPE. Although the cancer risk is only 20%, CFJ RUSSEL, in common with others advises surgical resection of all solitary thyroid nodules reported as follicular neoplasm cytologically. In this study 40 cases were diagnosed as follicular neoplasm cytologically and of these 4 were histologically malignant -10% cancer risk. Fenn & Krishnan 1976 & others found that there was no great sex predominance in the incidence of malignancy. A solitary nodule in very young patients almost malignant & in middle age it is rarely to be malignant and the incidence of malignancy increasing with the age told by Selwyn & Taylor in 1969.

The incidence of thyroid cancer in patients with a solitary thyroid nodule as follows

Study by Kendall & Condon 1969 } Pnarras et al 1972}	11-20%
Study by Colin F J Russell at Royal Victoria hospital, BELFAST., UK	13%
Study by Fenn & Krishnan at CMC Vellore, Tamilnadu	12.6%
Study by Nagori et al 1992	11%
Study by Dr.L.M.Mukerjee & Prof.M.C. Dandapet, MKG medical college, Berhampur Orissa	11.1%
Study conducted in Kilpauk Medical College, Chennai 2006-2008	13.33%

This compares well with the other studies on solitary nodule goitre.

The maximum incidence of malignancy of 29% of cases was present during the 4^{th} decade. The incidence of malignancy in females & males was almost equal in all decades from the 2^{nd} but the incidence in male was common in 5^{th} and 6^{th} decades in study by Lt Nagori in 1992.

TABLE-12

AGE & SEX DISTRIBUTION OF BENIGN AND MALIGNANT NODULE

AGE in years	MALES			FEMALES		
	BENIGN	MALIGNANT	TOTAL	BENIGN	MALIGNANT	TOTAL
Upto 20	1	1	2	2	1	3
21-30	1	0	1	21	0	21
31-40	1	0	1	22	3	25
41-50	2	2	4	7	0	7
51-60	1	1	2	7	0	7
60 & above	0	0	0	0	2	2
TOTAL	6	4	10	59	6	65

In our study 40% of solitary nodule in males proved to be malignant whereas in females only about 9% of the solitary nodules harboured malignancy. According to Matheson 1986, the malignant potential of a nodule in a man is approximately three times that for a woman of comparable age and in our study, the risk has been almost four times. In males 75% of cancer occurred in more than 40 years age group. Malignancy is more likely in a nodule in a child or a teenager or when goitre develops in

a patient aged 60 years & above (Hamming et al 1990, Caruso and Mazzaferri 1991).

50% of thyroid cancers occurred in individuals under 40 years of age and of them 80% of them is papillary carcinoma. Fravenhofer et al 1970 in his study of 125 cases of thyroid cancer found that 80% of thyroid cancers in individual less than 40 years of age were papillary carcinoma.

TABLE- 13

HISTOLOGICALLY PROVEN MALIGNANCY

TYPE	No OF PATIENTS	PERCENTAGE
PAPILLARY CA	8	80
FOLLICULAR CA	2	20
MEDULLARY CA	0	0

No medullary carcinoma, anaplastic carcinoma and lymphoma were reported in our series. The relative incidence of primary malignant tumors in our series is almost in accordance with most of the reported series.

SURGICAL PROCEDURES

CARCINOMA

We have done total thyroidectomy with or without neck dissection in five patients. All the five were papillary carcinoma. Near total thyroidectomy was done for a case, also of papillary carcinoma. Total thyroidectomy is considered not only as a measure to reduce the recurrence rate of differentiated carcinoma but also as a means of preventing development of a highly undifferentiated lesion. The percentage of radioiodine pick up can be increased several fold after total thyroidectomy and it is also increases the sensitivity of thyroglobulin as a postoperative marker of residual/recurrent disease.

DISADVANTAGE

The risk of permanent hypoparathyroidism or recurrent laryngeal nerve damage is high. We have done near total thyroidectomy for one patient, a case of cytologically proved papillary carcinoma, which was a small lesion (1.5cm) preserving one parathyroid. Indications for near total thyroidectomy, includes smaller lesions and better prognostic variants of papillary carcinoma.

Out of four false negative patients (cytologically benign) all were treated with Hemithyroidectomy. All these patients were taken up for completion thyroidectomy because they had an uneventful postoperative

period and follow up. In our study 3 patients with clinical toxicity were reported as follicular neoplasm and as follicular adenoma in HPE. Out of 75 cases operated 36 cases reported as adenoma in HPE report. Hemithyroidectomy done for all patients. 36% of operated cases were diagnosed as nodular goitre, Hemithyroidectomy done for most of them. 5 patients had nodules in the contra lateral lobe also, who were revealed peroperatively, and hence subtotal thyroidectomy was done.

OUT COME OF THERAPY

Complications:

Out of the 75 patients operated, two developed features of hypocalcaemia in the immediate postoperative period and were revived with intravenous, calcium gluconate and with no need for oral calcium supplementation.

Two patients had sluggish movement of left vocal cord after total thyroidectomy and improved later. Three patients had postoperative wound infection. We had no mortality during this study.

COMPARISON OF STUDY

Study by Colin FJ Russel FRCS at Royal Victoria Hospital Belfast, U.K 61 patients operated for solitary thyroid nodule			Study at Kilpauk Medical College Hospital Kilpauk Chennai 75 patients operated for solitary thyroid nodule	
FNAC Pathological Diagnosis	Number of patients	Percentage	Number of patients	Percentage
Nodular goitre	30	49	27	36
Follicular adenoma	19	31	36	48
Malignancy	8	13	10	13.33
Hashimoto's thyroiditis	3	5	2	2.67
Dequervains	1	2	-	-
Simple cyst	-	-	-	-

CONCLUSION

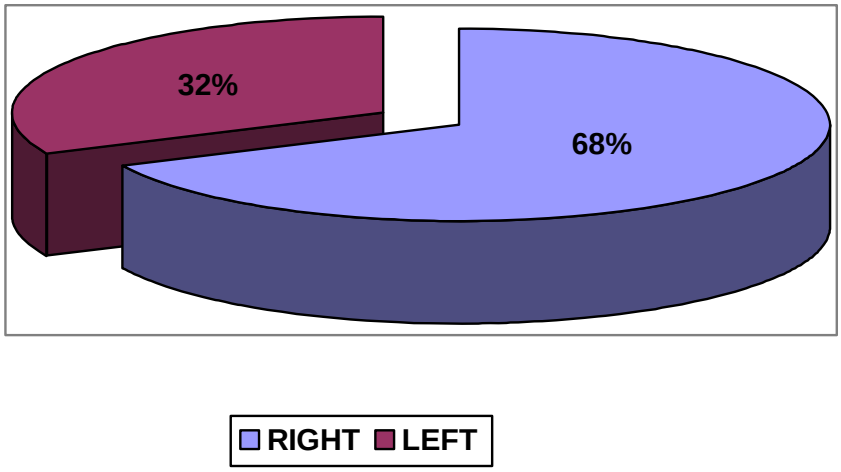
CONCLUSIONS

- From our study, the common causes of SNT are adenoma, a dominant nodule of MNG, Hashimoto's thyroiditis in the benign variety while papillary & follicular carcinomas were among the malignant causes.
- Among the SNT adenoma (48%) is the most common lesion & papillary carcinoma (80%) is the most common malignancy.
- The incidence of SNT is very high among females (87.5%) comparing with males (12.5%) but the malignancy rate is high among males (40%) comparing with females (9.2%).
- SNT more common in the right lobe (68%) than the left lobe (32%).
- The incidence of toxic symptoms in SNT is very less (3.75%).
- The incidence of malignant lesion is 13.33%.
- The incidence of SNT highest in the age group of 21-40 years with a 65% of patients falling in this age category.
- FNAC is the gold standard test for evaluating SNT with accuracy rate of 94.6%.
- USG & Radioiodine study are supplementary to FNAC.
- A surgical procedure in any form remains diagnostic as well as therapeutic even though the trend now is non-surgical management with close follow up for the most of the benign lesions.

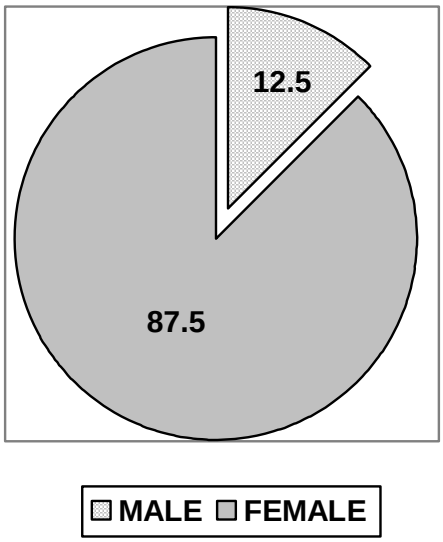
- HPE remains to be the final diagnostic proof. According to that results the management strategies varies.
- Follow up is essential in SNT because unlike other malignancies thyroid carcinoma are easily amenable to cure, have got better prognosis & prolonged survival rate.

Annexure

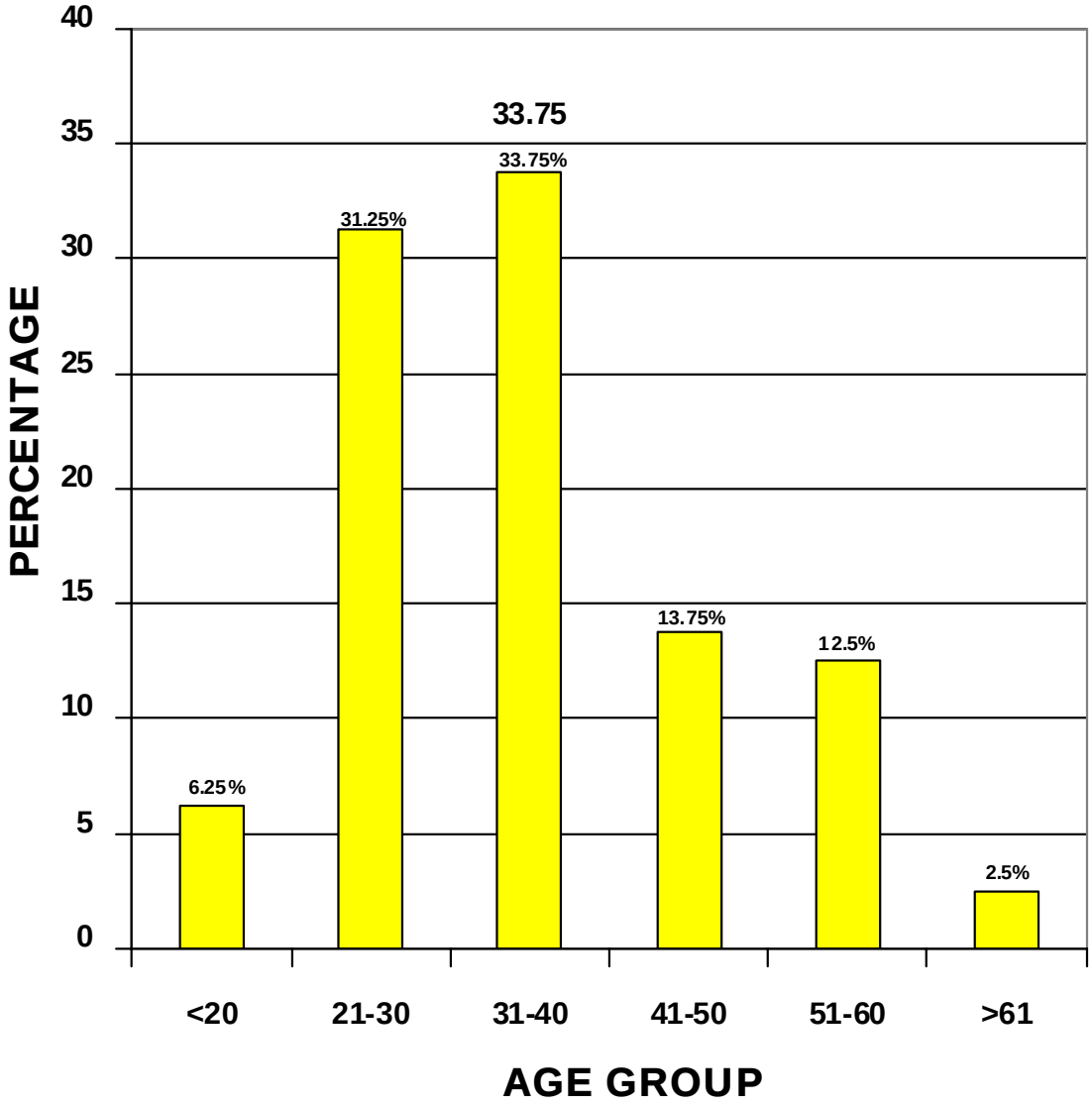
SIDE OF INVOLVEMENT IN SNT

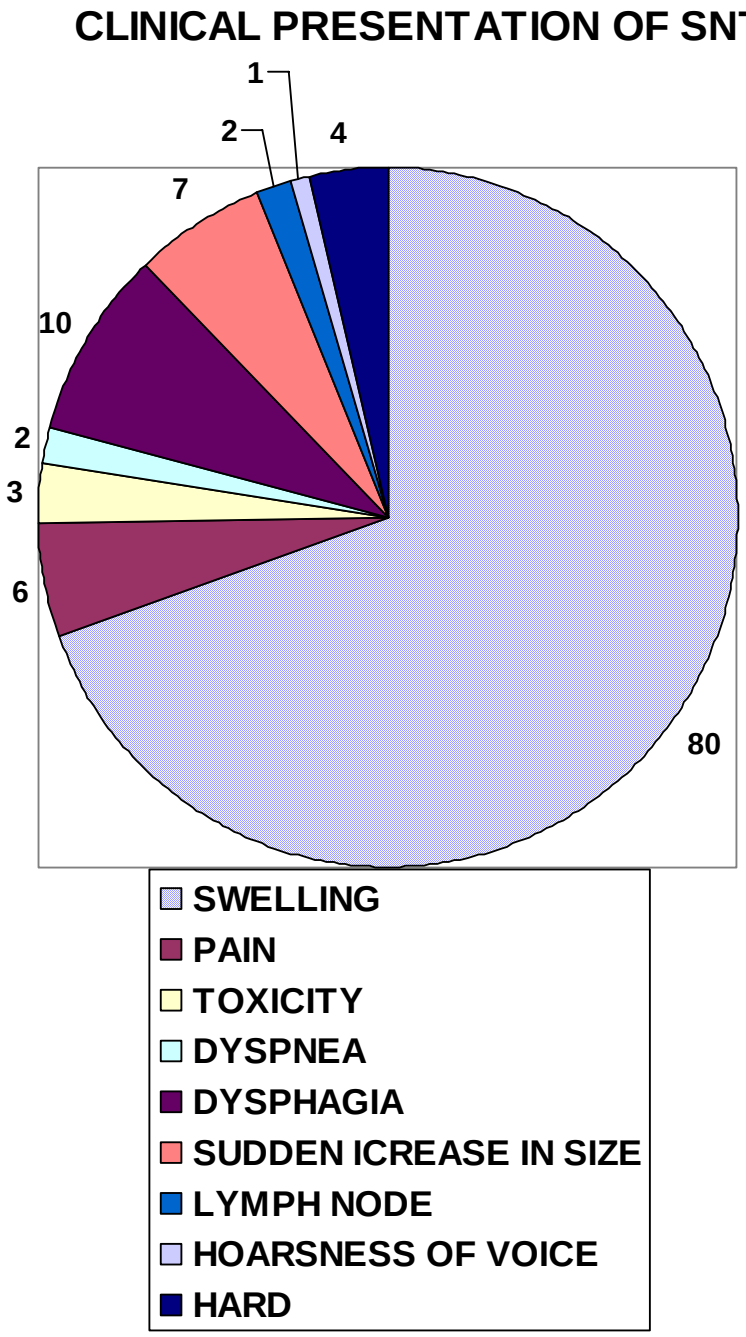


SEX DISTRIBUTION OF SNT

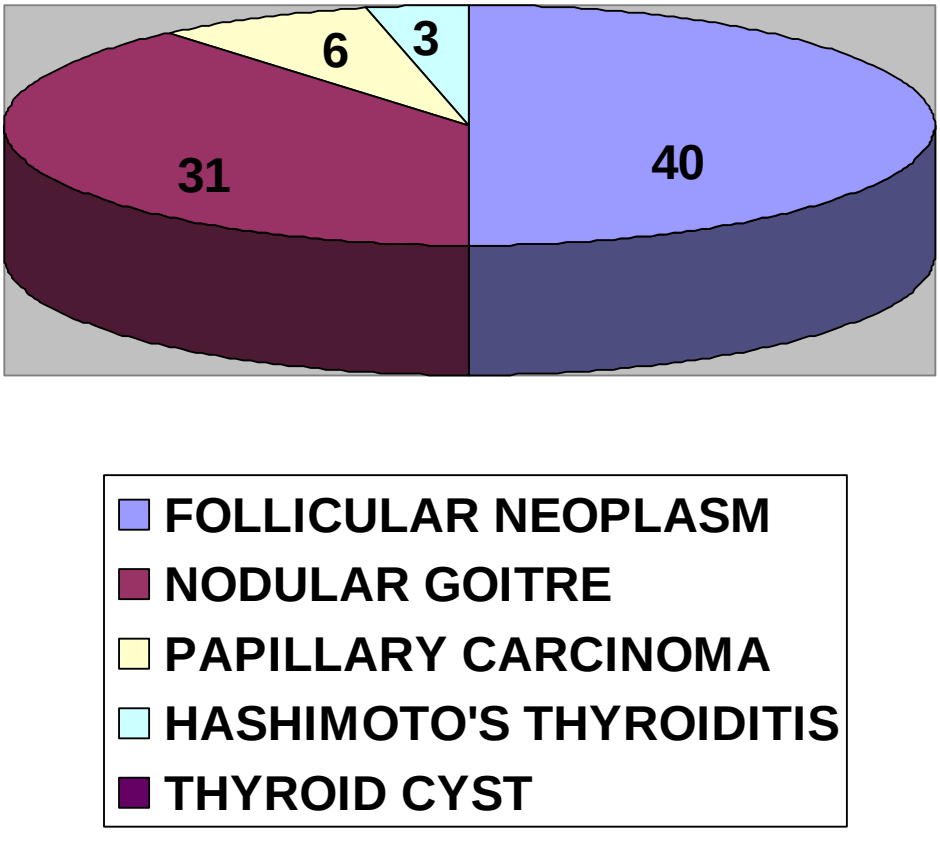


INCIDENCE OF SOLITARY NODULE THYROID ACCORDING TO AGE

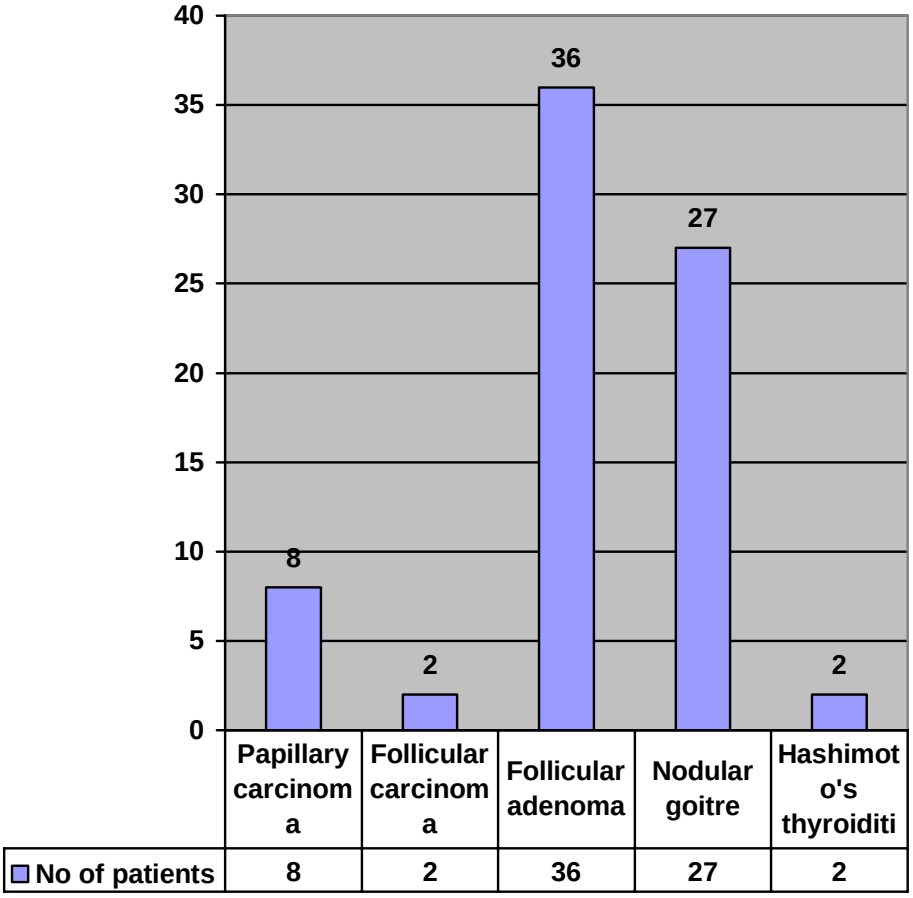


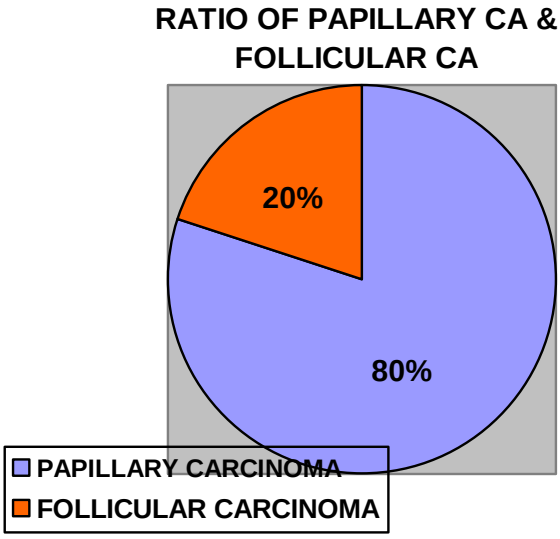

CLINICAL PRESENTATION OF SNT
1
2
4
7
10
2
3
6
80
SWELLING
PAIN
TOXICITY
DYSPNEA
DYSPHAGIA
SUDDEN ICREASE IN SIZE
LYMPH NODE
HOARSNESS OF VOICE
HARD

FNAC REPORTS

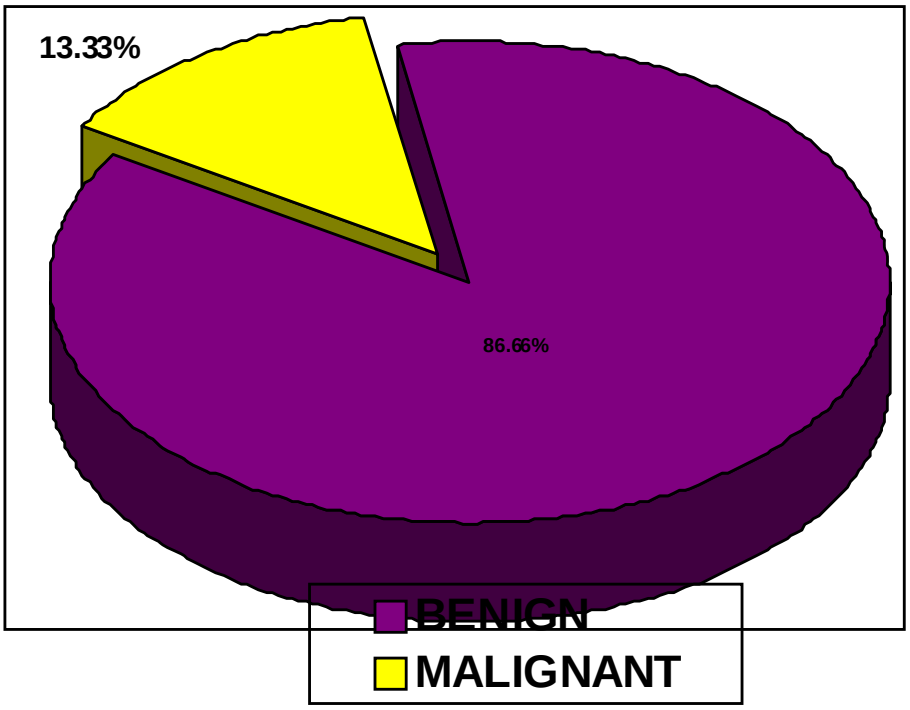


HPE REPORTS


40
35
30
25
20
15
10
5
0
36
27
8
2
2
Papillary carcinoma
Follicular carcinoma
Follicular adenoma
Nodular goitre
Hashimoto's thyroiditi
No of patients
8
2
36
27
2


RATIO OF PAPILLARY CA & FOLLICULAR CA
20%
80%
PAPILLARY CARCINOMA
FOLLICULAR CARCINOMA

SPECTRUM OF SOLITARY NODULE THYROID



PROFORMA

PROFORMA

A STUDY ON CLINICOPATHOLOGICAL EVALUATION OF SOLITARY NODULE OF THYROID

Age Sex Unit IP No.

DOS : DOD :

PRESENTING COMPLAINTS

Swelling - Onset

Duration

Rate of Growth

Associated Pain

Pressure Effect - Dyspnoea

Dysphagia

Hoarseness of Voice

Symptoms of Thyrotoxicosis

Symptoms of Hypothyroidism

History of irradiation of face and neck

Family history of Thyroid Malignancy

Any other systemic illness.

GENERAL EXAMINIATION

Pulse rate	:	Eye Signs
Blood Pressure	:	Skin Changes
		Tremors

LOCAL EXAMINIATION

Thyroid Swelling:

Site	:	Border	:
Size	:	Consistency	:
Shape	:	Movement with Deglutition	:
Surface	:	Mobility	:
Extent	:	Tracheal Position	:
Regional Lymph nodes	:		

SYSTEMIC EXAMINATION

CNS	:
RS	:
Abdomen	:
SKELETAL SYSTEM	:

PROVISIONAL DIAGNOSIS

INVESTIGATIONS

Haemoglobin	:	Urine analysis	:
Blood Sugar	:	Blood Urea	:
Serum Cholesterol	:	Thyroid Profile	:
Chest X ray	:	Xray neck	:
USG	:	CT Scan	:
IDL Scopy	:	FNAC	:
Biopsy report	:		

TYPE OF SURGERY :

POST OPERATIVE COMPLICATIONS:

ABBREVATIONS

ABBREVATIONS

FA → FOLLICULAR ADENOMA

NG → NODULAR GOITRE

HASHI → HASHIMOTO'S THYROIDITIS

FOLL CA → FOLLICULAR CARCINOMA

PAP CA → PAPILLARY CARCINOMA

HT → HEMITHYROIDECTOMY

CT → COMPLETION THYROIDECTOMY

NTT → NEAR TOTAL THYROIDECTOMY

TT → TOTAL THYROIDECTOMY

LND → LYMPH NODE DISSECTION

p → present

MASTER CHART

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MASTER CHART

Sl.No	Name	AGE	Sex	IP No	Clinical Presentation									Side	FNAC	HPE	Management
					swelling	Pain	Toxicity	Dyspena	DYSPHAGIA	SUDDEN INCREASE IN SIZE	LYMPH NODE	HOARSNESS OF VOICE	HARD CONSISTENCY				
1	Vimala	19	F	23127	p									L	FA	FA	HT
2	Jeyasheela	19	F	22779	p									R	FA	PAP CA	CT
3	Kanimozhi	18	F	19292	p									L	FA	FA	HT
4	Charles	19	M	25568	p									R	NG	NG	HT
5	Ramamoorthy	20	M	14192	p				p		p			L	PAP CA	PAP CA	TT & LND
6	Shanthi	27	F	16984	p									R	NG	NG	HT
7	Sumathi	23	F	10440	p									L	FA	FA	HT
8	Sabiya	25	F	27814	p			p						R	NG	NG	HT
9	Roopini	21	F	28841	p									L	NG	NG	HT
10	Amudha	28	F	5863	p									R	FA	FA	HT
11	Malathy	29	F	14837	p									L	NG	NG	STT
12	Tamilselvi	27	F	15732	p									R	FA	FA	HT
13	Devi	30	F	21727	p		p							L	NG	NG	STT
14	Sunitha	29	F	23562	p			p						R	FA	FA	HT
15	Selvi	22	F	21323	p									L	NG	NG	STT
16	Uma	30	F	1487	p									L	FA	FA	HT
17	Parvathy	27	F	3066	p									R	NG	NG	HT
18	Meharnisha	26	F	7518	p		p							L	FA	FA	HT
19	Kalarani	28	F	13901	p									R	FA	FA	HT
20	Selvi	30	F	14946	p				p					L	FA	FA	HT
21	Malathy	26	F	16886	p									R	FA	FA	HT
22	Regina	29	F	19273	p	p								R	FA	FA	STT

23	Rani	25	F	23735	p									L	NG	NG	STT
24	Mahalakshmi	23	F	12931	p		p							L	NG	NG	HT
25	Lakshmi	23	F	14225	p				p					L	FA	FA	HT
26	Sundarammal	30	F	16732	p	p								L	NG	NG	HT
27	Anitha	26	F	25569	p									L	NG	NG	HT
28	Shakila	21	F	29450	p									R	FA	FA	HT
29	Bhuvana	24	F	13626	p									R	NG	NG	HT
30	Ramu	22	M	20045	p									R	FA	FA	HT
31	Sherli	34	F	29073	p									R	FA	FA	HT
32	Rajeswari	40	F	13696	p									L	FA	FA	HT
33	Asothai	33	F	21286	p									R	PAP CA	PAP CA	TT
34	Latha	35	F	23481	p									R	NG	NG	HT
35	Kanaga	38	F	11015	p	p			p					R	FA	FA	HT
36	Manonmani	36	F	22397	p									R	NG	NG	HT
37	Baunumathy	37	F	15172	p									L	FA	FA	HT
38	Gowri	37	F	17338	p									R	NG	NG	HT
39	Shanthi	32	F	18406	p	p								R	HASHI	HASHI	HT
40	Thulasi	40	F	21439	p					p				R	NG	NG	HT
41	Mallika	39	F	24637	p				p					R	NG	NG	HT
42	Rohini	32	F	22624	p									L	FA	FA	HT
43	Valli	36	F	27159	p									R	FA	FA	HT
44	Visalammal	33	F	496	p									R	NG		Conservative
45	chinammal	38	F	3830	p								p	R	FA	FOLL CA	CT
46	Gnanaselvi	32	F	8844	p									R	NG		not willing
47	Natarajan	35	M	13077	p									L	NG	NG	HT
48	Selvi	39	F	16650	p	p								R	HASHI	HASHI	HT
49	Indhra	36	F	20497	p				p					R	NG	NG	HT
50	Bommi	35	F	20515	p									L	FA	FA	HT
51	dhanam	35	F	21280	p									R	FA	FA	HT
52	usharani	37	F	14582	p									R	FA	PAP CA	CT
53	mary	38	F	20010	p									L	NG	NG	HT
54	Jeyanthi	34	F	37701	p									R	NG	NG	HT
55	Karuna	40	F	29073	p	p								R	FA	FA	HT
56	Latha	36	F	23456	p									R	FA	FA	HT
57	Meena	37	F	25679	p									R	FA	FA	HT
58	Pandiyan	44	M	250281	p									R	FA	FA	HT
59	Karupasamy	42	M	26791	p									L	PAP CA	PAP CA	NTT

60	Murugesan	45	M	17173	p									R	FA	FOLL CA	CT
61	Rasul	47	M	20045	p					p				R	NG	NG	HT
62	Rajammal	45	F	7368	p					p				R	NG	NG	HT
63	Guna	48	F	8951	p									R	FA	FA	HT
64	Varadamal	50	F	9846	p					p				L	NG	NG	HT
65	Vatchala	45	F	27658	p									R	FA	FA	HT
66	Valli	45	F	6917	p					p				R	NG	NG	HT
67	Fathima	42	F	6366	p									L	FA	FA	HT
68	Jeyalakshmi	45	F	1393	p									R	FA	FA	HT
69	Puspha	59	F	1067	p									R	FA	FA	HT
70	Jeya	57	F	16811	p									R	NG		Conservative
71	Sivakami	53	F	17980	p			p						R	FA	FA	HT
72	Rose	54	F	9719	p									R	NG	NG	HT
73	kupammal	58	F	10537	p									R	FA	FA	HT
74	Meera	55	F	38112	p									R	NG		Conservative
75	Lakshmi	60	F	4702	p									R	FA	FA	HT
76	Manju	60	F	26140	p									R	FA		not willing
77	jaya	57	M	2148	p				p		p		p	L	PAP CA	PAP CA	TT & LND
78	Subramanian	55	M	2262	p									R	FA	FA	HT
79	Govindammal	61	F	8746	p					p			p	R	PAP CA	PAP CA	TT
80	Lakshmi	63	F	8482	p				p	p		p	p	R	PAP CA	PAP CA	TT